Depression, anxiety, schizophrenia and bipolar disorder are highly prevalent mental health problems across the globe (1). While distinct in many respects, disabling low mood or negative affective state are common to all these neuropsychiatric conditions. Understanding the mechanisms underlying such a transdiagnostic symptom is crucial in providing insight into the pathogenesis of these conditions and for optimising clinical management procedures. In tandem, the development of more sensitive assessment tools to detect and monitor these symptoms is critical in enabling potential interventions to be deployed at the earliest possible stage.

Major obstacles to the effective exploration of mood-related symptoms in neuropsychiatric illness include the lack of animal models that comprehensively recapitulate human symptom presentation, the limited number of assessment tools to evaluate affective state in non-human species and, where such tools do exist, the lack of similarity between them and the methods used in the clinic or in human research. This has led to the conceptualisation of a “translational gap” between animal and human studies which may contribute to the considerable levels of clinical trial failure in the neuropsychiatric therapeutic development area, with compounds found to be promising based on preclinical data ultimately proving to be ineffective in the clinical context.

Closing this “translational gap” is therefore a high priority and to contribute to this effort, this project is focused on two questions:

- When studying “affective-state” in the content of neuropsychiatric disease, are we currently translating relevant information between rodent model systems and the clinical context?

- At a more fundamental level, are we actually evaluating the same emotion-related processes in the preclinical and clinical systems?

Project overview:

Characterisation of mood/affective state often requires subjective description by the individual experiencing it. While this is possible in patients who can use language, access to such information from non-verbal animal models is impossible. However, recent research has suggested that commonality in a construct referred to as ‘Cognitive Affective Bias’ (CAB) exists between species and that this can used as a platform for translational studies of mood.

The basis of CAB concerns the way an organism interprets ambiguous/uncertain stimuli in their environment given their overall affective state. For example, depressed patients are more likely to remember negative rather than positive emotional information in self-relevant tasks and interpret key social signals, such as facial expressions, as either more negative or less positive than healthy volunteers (2,3). Negative CAB has also been linked to increased risk of relapse (3) and vulnerability to depression even in people who have never previously been depressed (6). Beyond depression, people with high neuroticism personality trait scores (4–6) and people with anxiety (7) also exhibit negative bias or “pessimism”, demonstrating potential transdiagnostic value in CAB.

In the preclinical context, several different tasks to measure CAB have been developed for rodents using mazes, operant chambers with levers or touchscreen manipulanda (8–11). Our laboratory has also developed a CAB task for the rodent touchscreen system with high similarity to a task already available for non-human primates (12), which may ultimately translate more reliably for use in humans.

In general, CAB tasks require animals to assign an affective state “value” to different stimuli: “positive” (e.g. to a stimulus associated with reward delivery) or “negative” (e.g. to a stimulus associated with a noise, a flashing light or a “time out”). Once they learn this “emotional dichotomy” they are presented with ambiguous stimuli (i.e. stimuli that share varying degrees of similarity with the “positive” or “negative” stimuli) and they respond to these according to their...
expectations. These tasks are sensitive to pharmacological manipulations known to impact mood, with animals increasing their responses to the ambiguous stimuli after the administration of antidepressants (“optimistic bias”) and decreasing their responses to ambiguous stimuli after the administration of pro-depressant drugs (“pessimistic bias”).

In contrast, current CAB tests used in humans are typically based on the presentation of words with different emotional valences (13) and on the recognition of facial expressions (5), processes which are not accessible in rodent model systems.

In this project, we therefore aim to develop a series of touchscreen-based tasks for assessing CAB in humans. These tasks will mimic the available preclinical touchscreen CAB task designs to maximise their translational potential. Once developed, these tasks will then be validated through comparison against questionnaires and other measures of mood that reliably detect CAB in humans.

Techniques:
A wide range of cutting edge behavioural and cognitive assessment resources will be available for this project. The studentship will be based at the OU campus in Milton Keynes but there may be opportunities to conduct elements of this project at collaborating institutions.

Funding information:
This three-year research studentship is funded by the Faculty of Science, Technology, Engineering and Mathematics (STEM) at The Open University and provides a stipend of £15,009 per year (2020 rate) and all academic fees (at UK/EU level) are covered.

The project is supervised by Drs Laura Lopez-Cruz, Christopher Heath and Paola Fuentes-Claramonte. The student would be required to live in the UK and within commuting distance of The Open University in Milton Keynes.

Requirements:
Applicants will be expected to have a good undergraduate degree (upper second class or higher) in Psychology, Neuroscience or a related discipline.

It would be advantageous to have some experience with:
- Applying quantitative methodologies (e.g. cognitive tasks and questionnaires) to evaluate cognition (particularly affective state-related constructs).
- Cognitive task design and programming (e.g. using Python, Psychopy, Matlab or other relevant software)
- Research involving animal models (rodents) and/or neuropsychiatric patients.

Contacts:
Informal enquiries relating to the project should be directed to Laura.lopez-cruz@open.ac.uk

How to Apply:
Please send an email with your CV, a completed application form and a personal statement (outlining your suitability for the studentship, what you hope to achieve from the PhD and your research experience to date) to STEM-LHCS-PhD@open.ac.uk.

Closing date: 7th February 2020

Interviews will be arranged promptly after the closing date, and can be conducted via Skype if appropriate.

LHCS holds Athena Swan Bronze status

Equal Opportunity is University Policy

References:
