BRITISH PHARMACOLOGICAL SOCIETY

Laboratory Animal Science Association

Psychiatry Consortium

EXPLORING THE STATUS OF ANIMAL MODELS OF PSYCHIATRIC DISORDERS WITH BPS, LASA AND THE PSYCHIATRY CONSORTIUM - MY EXPERIENCE

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The joint seminar and workshop of the British Pharmacological Society (BPS), Laboratory Animal (LASA) and Psychiatry Consortium was held on the 24th and 25th February 2021, with the theme "Exploring the status of animal models of psychiatric disorders - their validity and scope for successful translation." The focus was on the challenges and opportunities in pre-clinical translation of new therapeutics for psychiatric diseases. Erudite scholars and investigators in the various aspects of psychiatry, delivered seasoned lectures in selected areas covered during the seminar and workshop. The various speakers were well experienced in their given topics.

The seminar was made up of four sessions;

1. **Paula Moran spoke on translational relevance of preclinical studies relevant to schizophrenia.** She took us down memory lane from when schizophrenic states were induced in animals using D-amphetamine or apomorphine to the current practice where cell cultures are used to identify specific biomarkers implicated in schizophrenia, which could be useful therapeutic targets. Paula Moran concluded by stating that a research domain criteria (RDoC) approach may help to better align the behaviour relevant to disease rather than trying to replicate the whole disease and also enable new developments in neuroscience and affiliated fields to be incorporated and refine existing methods. Secondly, she added that the more information we can add from clinical studies back to animal studies and vice versa, the more precisely we can refine our methods.

2. **Michaella Filiou also spoke on "From animals to omics in psychiatry research".** She shared her research experience from their laboratory on proteomics and metabolomics in identifying targets for stress management. One of the products from this research area is uncovering the role of mitochondria in the management of stress.

Cathy Fernandes spotlighted the role of epigenetics and its implications for preclinical psychiatry research. She pointed out challenges for modeling in psychiatry, which include but are not limited to; gene-environment interplay and individual variation. These epigenetic regulations and manipulations can be explored as therapeutic targets in several disease conditions.

Pat Nolan shed light on individual differences in the rodent behaviour. He clearly pointed out that most physiological factors vary as a function of time. He stressed that environmental factors have strong influences on body clock time and several disturbances are associated with many psychiatry diseases. Therefore, researchers must keep these factors in mind, when planning and executing experiments.

3 **Session three started with a plenary lecture titled "The Microbiome in pre-clinical psychiatry.** Philip Burnet took us through a journey of the role of microbiome in mitigating psychiatric conditions, largely via the gut brain axis. He also shared his work, showing the anxiolytic, cognitive and anti-inflammatory effect of multi-species prebiotic/probiotic in mice. Jason Rihel also talked about using zebrafish to study complex behaviours. His fascinating work essentially studies the gene phenotypic pipeline, systematically generating mutants in the genes, analyzing and mapping behaviour in neuro-circuits or changes in synaptic structures and finally doing an intervention using drugs via in vivo studies in the zebrafish to identify circuits that can be rescued pharmacologically.

4 **In the fourth session, Paul Finnemore extensively discussed laboratory stressors and the science of animal welfare – together with their implications for translation.** The direct and contingent sufferings were mentioned, in that these stressors should be minimized as much as possible in animal experiments at all levels because they can affect the data we obtain in preclinical experiments.

The workshop, on the following day, comprised three sessions with several breakout rooms to give participants time to discuss and bring feedback to the main room.

1 **During the first session, the translatability of preclinical models in psychiatric drug discovery was discussed.** In the first breakout session, my group discussed "what criteria should be taken into account when considering the validity of a preclinical model of a complex, multifactorial disorder in humans?" We agreed that good knowledge of the disease condition, reproducibility and the species of animals that are studied are essential considerations.

2 **Session two highlighted key considerations when using translatable preclinical models in psychiatry.** Immediately after returning from the virtual coffee break, the session chair led the discussion on the top considerations when using preclinical models and the reasons behind such choices.

3 **Meanwhile session three emphasized "the future of preclinical models in psychiatry" and where we go from here.** Questions arising from group discussions were adequately addressed either by other participants or the Chair of that particular session. I especially enjoyed Clare Stanford's lecture on an "Introduction to the use of preclinical models in psychiatric drug discovery".

In summary, the key take home messages I gained from both the seminar and workshop were:

- In modeling psychiatric conditions using experimental models, a good understanding of the biological basis of the disease condition is crucial.
- For effective translatability, reproducibility of data is important.

- In the study of psychiatric disorders, researchers should look into specifics in the disease model instead of taking a holistic approach in addressing a whole, complex condition. For example, when looking at depression, a researcher can decide to measure cognitive deficit, anhedonia etc.
- Metabolomics or proteomics studies can be helpful in the discovering therapeutic targets in psychiatric disorders.
- Apart from cell culture, mice, rats and zebrafish have also been explored to study complex behaviour.
- Laboratory stressors, whether direct or contingent, should be kept as minimal as possible.
- Researchers should keep in mind epigenetic considerations in translational study in psychiatry.

Finally, I was able to attend this year's joint meeting owing to the benevolence of a Psychiatry Consortium Support Grant, which I received as an Early Career Researcher to support my career development.

"Sincerely, I do really appreciate that kind gesture. I am most grateful to the organizers and funders who, through these workshops and similar events, have improved my understanding of research and ethics in translational psychiatric research."

About the Psychiatry Consortium Early Career Support Grant

The Psychiatry Consortium is a strategic collaboration of leading medical research charities and pharmaceutical companies focusing on the challenge of identifying and validating novel drug targets to address the unmet therapeutic needs of the people living with mental health conditions. Wellcome provides grant funding to the Psychiatry Consortium to support academic outreach activities which nurture academic interest in mental health translational research and engage the psychiatry academic community globally.

The Early Career Support Grant enables early career researchers to attend Psychiatry Consortium-led events and workshops. The grant is aimed at individuals who are in the early stages of their career and are looking to develop their professional network and expand their knowledge and skillset.