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The importance and depth of reproducibility in rodent models of psychiatric diseases

Scientific rigor is a fundamental aspect to the scientific method. Public and scientific opinion on such rigor has been negatively impacted recently with reproducibility concerns been covered in the press. From initial concerns that 42 of 50 major findings in *Nature* could not be reproduced, a survey of 1,576 researchers conducted by *Nature* revealed that > 70% of researchers failed to reproduce other scientist's experiments (Baker 2016). Failure to reproduce major findings in prestigious publications has been disconcerting - the pressure to publish and the selective reporting of results were two factors that the majority of respondents (> 60%) identified as contributing to such difficulties (Baker 2016). The Open Science Collaboration (OSC) failed to reproduce many results with significant findings, half of those originally reported (OSC 2015). Issues on reproducibility were covered in a recent review by lead researchers in the field after a meeting to discuss reproducibility in the field (Kafkafi et al. 2018). Beyond those general topics, this special issue has highlighted opportunities for reproducibility across various domains of research.

The papers in this special issue address a number of critical concerns related to reproducibility in work with animal models. It was our goal to try and shed some light on very different aspects of research in animal models of neuropsychiatry but center on the issue of reproducibility. Specifically, the paper by Michel Bourin re-examines some very common behavioral tests for anxiety and the possibility of using these tests more than once (Bourin 2018). The paper demonstrates that at least for some of these common tests, repetition of the tests in the same animals reduces their validity. Another common source of inconsistency that had been suggested as a possible cause for lack of reproducibility is the time in the day when experiments are conducted. To address this issue, Richetto and colleagues (Richetto et al. 2018) show that the time of testing (as it relates to light and dark phases) indeed has a major influence on behavior and on some biochemical correlates in the brain. Zebrafish are a relatively new model animal for studies related to neuropsychiatry and Robert Gerlai thoroughly examines specific issues or reproducibility related to this novel model animal with practical suggestions on how to overcome some of the problems (Gerlai 2018). Another set of unique challenges in the context of reproducibility are related to animals with targeted mutations. In this context, the paper by Kwiatkowski and colleagues (Kwiatkowski et al. 2017) is highly encouraging as it demonstrates that when critical parameters are maintained, the behavior of mice with targeted mutation in a relevant and translational model can be reproduced across time, and that the reproducibility is not just at the qualitative level but also across strains and when effect sizes are compared. The paper by Szumlinski and colleagues uses the Drinking-In-The-Dark (DID) murine model of binge-drinking, to examine additional two issues that are central to reproducibility, sex and age. In this paper, the authors clearly demonstrate that when other major factors are controlled for, there are consistent and reproducible differences between the sexes and between adolescent and mature mice in this model. This work highlights the need to use both sexes in studies and to strictly control for age. Lastly, the paper by Stukalin and Einat (Stukalin and Einat 2017) addresses another angle, the proper statistical analysis of data. Specifically, much work with animal models of neuropsychiatric disorders includes batteries of behavioral tests in the same animals and the paper suggests a statistical approach to such batteries that can emphasize overall differences between groups without overestimation due to multiple comparisons

Whereas there are undoubtedly a large number of factors that negatively affect reproducibility of experiments in general, we suggest that the papers in this special issue emphasize some of the important, albeit less discussed, problems that one needs to be aware of when designing experiments and when attempting to replicate previous results. We believe that addressing these issues in our everyday work can increase the validity and the reproducibility of our experiments with animal models of neuropsychiatric disorders and advance our attempts to explore the underlying biology of these devastating disorders as well as develop better treatments for them.

Conflicts of Interest

None.

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