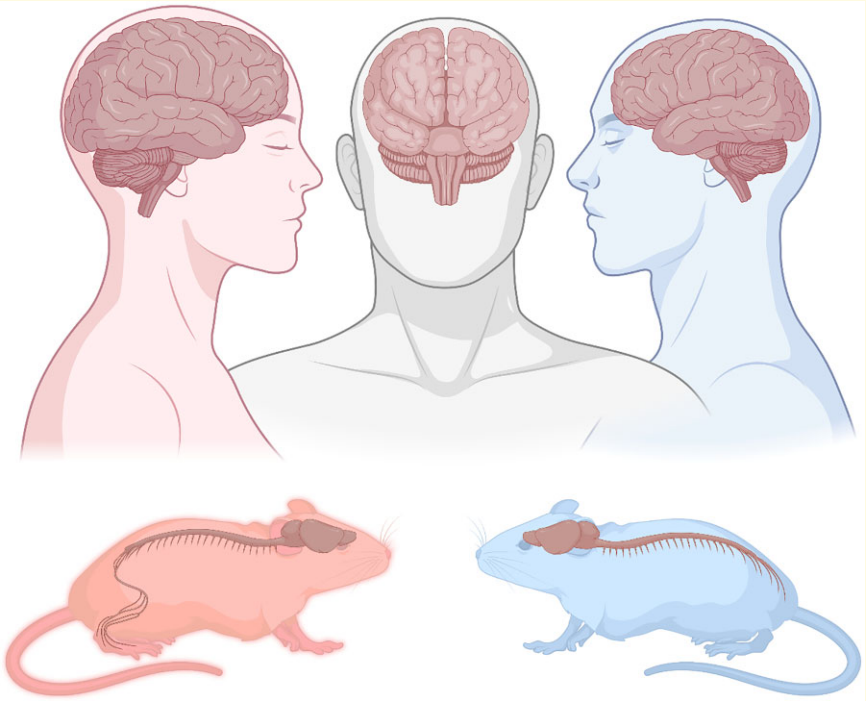
BRAIN COMMUNICATIONS

EDITORIAL

# Let's talk about sex (in translational neuroscience)

**Graphical Abstract**



Welcome to Volume 4, Issue 2 of *Brain Communications*. For this editorial, I would like to discuss the importance of sex and gender in neuroscience research, an issue that pops up in many aspects of neuroscience from papers to funding to clinical trials to recruitment and retention of neuroscientists. This issue is confounded from the start by the words 'sex' and 'gender' which are often used interchangeably. Here, I will talk about sex as a biological trait of humans and animals and gender as whether a person identifies as male, female, non-binary, transgender, etc. Neuroscientists have been aware of structural and functional differences between male and female brains in many species for decades.[1] These differences are biologically fascinating, like the example of sex differences in specific brain regions of bird species in which males sing but females do not.[2] In the translational neuroscience space, looking for sex differences in fundamental research in animals and consideration of gender balance in participants in clinical research in humans becomes very important for translation of research into clinical benefit for all people affected by conditions. Further, many neurological and psychiatric conditions have disparities in incidence between sexes.

Historically, rodent neuroscience work was performed in only male animals to reduce costs and variability, based on the assumption that female rodents are more variable than males due to the oestrous cycle. However, the data do not hold up this assumption; in fact, when studied directly, including females does not increase variability in neuroscience studies and for most studies, the oestrous cycle does not have an effect.[3] Indeed in a meta-analysis of over 26 000 mice, sex

Received February 7, 2022. Revised February 7, 2022. Accepted February 8, 2022.

bias in variability was trait dependent with some traits more variable in males and some in females.[4]

Women are under-represented in clinical trials for neurological conditions,[5] despite increased incidence in females of some of these diseases such as Alzheimer's disease. This has significant effects on people who use approved drugs from these biased trials. For example, after the sleeping pill zolpidem was approved, it was observed that blood levels of the drug were 25–33% higher in women than in men, which can increase the risk of impaired driving the next day.[6] Transgender and non-binary people also face significant health disparities and there is an almost complete lack of inclusion of these groups in medical research.[5]

In the global neuroscience research environment, increasingly, there are policies to mandate the inclusion of sex as a biological variable in fundamental research and to improve the inclusion of women in clinical research (although I cannot find much evidence of progress in the inclusion of non-binary or transgender individuals). Since 2016, the National Institutes of Health in the USA has required consideration of sex as a biological variable in grants that they fund as part of their ongoing efforts to improve rigour and scientific reproducibility.[7] The Medical Research Council in the UK has not yet included a policy on sex as a biological variable in their funded work, but this is being discussed. Both the EU Clinical Trials Regulation and US Food and Drug Administration (FDA) now have policies requiring the inclusion of representative population groups in clinical research including gender. Surprisingly, the FDA only lifted its ban on women participating in clinical research by an act of congress in 1993![6]

Issues of gender are also present in the neuroscience workforce and, relevant to this article, in publishing. Around half of neuroscience students and one-third of faculty in neuroscience are women, and gaps persist in salary and promotions. Trans and non-binary faculty are even more rare, so much so that I cannot find numbers for this, although I have read that in 2013, Ben Barres was the first openly transgender scientist elected to the US National Academy of Sciences.[8] In publishing, a study of neuroscience journals between 2005 and 2017 found underrepresentation of women, particularly in high-profile journals.[9] There was a particularly unpopular paper published in November 2020, which suggested that having a female lead author was detrimental to the careers of early-career scientists. The outrage on social media led to the retraction of this paper 1 month later.[10] This type of controversy in the publishing space led us to some introspection about our practices at *Brain Communications* and whether we should attempt things like double-blind peer review. Before changing policy, our scientific editor Dr Manuela Marescotti and intern Flavia Loreto looked through our data for any signs of gender bias from our editorial team or reviewers. Keep an eye out for an upcoming Field Potential article reporting the results. Slight spoiler alert, I am proud of how the results turned out.

Another part of *Brain Communications*' effort to enhance rigour and reproducibility in this part of translational neuroscience is our policy on stating the sex of participants/subjects in all of the papers published in *Brain Communications*. Our editorial team checks every paper before acceptance to be sure this is clear and requires authors to explicitly state that inclusion of a single sex/gender in any study is an important limitation.

This short article barely scratches the surface of the issues of sex and gender in neuroscience. We would love to hear what you think, so join the conversation on Twitter with @BrainComms or send in a letter to the editor if you have good ideas.

The graphical abstract associated with this editorial was created with BioRender.com.

The cover image for this issue comes from Dr James Catterson, and shows a confocal image of a whole fly expressing trans-tango to label pre-synaptic pigment dispersing factor neurons (cyan) and all of the synaptically connected downstream neurons (magenta).

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