

## “Harnessing the Power of Sex Differences: What a Difference Ten Years Did Not Make”

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**Abstract:** Sex differences exist in many neurological and psychiatric diseases. Mandates have been initiated across funding agencies for research to include males and females. What has been lacking in the literature is a detailed assessment of how sex is incorporated into the design (e.g. balanced design) and into the analyses (e.g. covariate). We surveyed papers in 2009 and 2019 across six journals in Neuroscience and Psychiatry. There was a 30% increase in the percentage of papers that included both sexes to 68% in 2019. Despite this increase, in 2019 only 19% of studies used an optimal design for discovery of possible sex differences and only 5% analyzed sex as a discovery variable. Here we show that little progress has been made in harnessing the power that sex differences can afford in research for discovery and therapeutic potential for neurological and psychiatric disease to improve the health of men, women and gender diverse individuals.

**Impact:** This paper shows that despite an increase in the number of papers including both sexes, an alarmingly low amount are actually appropriately analyzing their data to detect sex differences. Further, among single-sex studies, gaps in our understanding of female health remain – with male-only papers being 9x more common than female-only papers. While the efforts that funding agencies have made to require that both sexes are used in studies are appreciated and an important step in the right direction, this study shows there is still a large amount of room for improvement in how researchers design their studies and analyze their data. This paper will be helpful for researchers, grant reviewers, and journal reviewers to think carefully about how to design well-powered studies, with equal sample sizes for each sex, and making sure their planned analyses are optimized to test for sex differences and interaction effects.