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Sex Differences in Molecular Rhythms in the Human Cortex

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To tweet: What does the time of day have to do with molecular sex differences in the brain? This paper examines similarities and differences between men and women using post-mortem cortical brain regions and uncovers sex differences in transcriptional rhythms.

There has been controversy over the existence of sex differences in the human brain based on studies of structure size, activity and connectivity. However, sequencing studies identified wide scale region specific sex differences in both humans and animal models. Often these transcriptional sex differences are uncovered when we examine the brains of people who experienced mental illness. This paper examines postmortem tissue from neurotypical cis gendered individuals and supports another important and often overlooked form of region-specific transcriptional sex differences in the human brain. Using the time of death normalized to the zeitgeber time scale, the authors examined sex differences in diurnal rhythmicity of gene expression in the dorsolateral prefrontal cortex and anterior cingulate cortex from post mortem male and female brains. They found that the canonical circadian genes did not differ between the sexes however, when they looked at widescale transcriptional gene expression, they found sex differences in the rhythmicity in both brain regions. In addition, they identify that males had almost twice the phase concordance between these regions compared to females. Their work also supports that there are different upstream regulations of sex specific transcriptional rhythmicity. Overall, their data highlights how important time of day is to understanding what sex differences in transcriptional regulation mean for the brain and the individual.