Sex Differences in Tyrosine Hydroxylase Expression Within the Norepinephrine System of the A1 Anatomical Region in Mice

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Norepinephrine System: • Noradrenergic neurons are a group of neurons originating in the focus coeruleus of the brainstem and are involved in the regulation of several physiological and behavioral functions. • These neurons release the neurotransmitter norepinephrine (NE) and play a significant role in modulating various brain functions, including attention, arousal, anxiety, and stress responses. • Dysfunctions in the noradrenergic system have been implicated in several psychiatric and neurological conditions, including Parkinson’s disease and Major Depressive Disorder.

Tyrosine Hydroxylase: • NE neurons express the enzyme tyrosine hydroxylase (TH), which is required for the synthesis of catecholamines, including dopamine, noradrenaline, and epinephrine. TH is the rate-limiting enzyme in the biosynthesis of catecholamines and is considered a biomarker of noradrenergic neurons.

A1 Anatomical Region: • Noradrenergic neurons are primarily located in two regions of the brainstem, the locus coeruleus (LC) and the A1 region. The LC is the largest noradrenergic nucleus in the brain and is involved in the regulation of several physiological and behavioral functions, including the sleep-wake cycle, attention, and stress responses. • The A1 region is a smaller nucleus located in the rostral ventrolateral medulla and is involved in the regulation of cardiovascular function and blood pressure.

Project Significance

Gaps in Neuroscience Research Regarding Sex Differences:

• For a long time, research in neuroscience largely focused on male subjects with the assumption that the findings would also apply to females. However, there are fundamental sex differences in the anatomy and function of noradrenergic neurons.
  o Greater noradrenergic neurons in the LC of males compared to females
  o Greater stress response in males

• These findings suggest that the noradrenergic system may contribute to the sex differences observed in neurological disorders. By studying sex differences in neuroscience, researchers can develop a more nuanced understanding of how the brain works and how to develop more effective treatments for both men and women. This knowledge can ultimately lead to better healthcare outcomes for all patients, regardless of their sex.

Goal: To compare sex differences in tyrosine hydroxylase and norepinephrine expression in the A1 region and relate findings to neurological disorders.

Hypothesis: We hypothesized that TH expression will be greater in female A1 regions rather than male A1 regions. This hypothesis was built upon findings from previous studies suggesting that female hormones, such as progesterone, increase A1 norepinephrine neurons’ activity and TH expression.

Research Goal and Hypothesis

Methods

Conclusions and Future Directions

• The results support our hypothesis that females exhibit greater TH expression in the A1 region compared to males.
• This has important implications because many neurological disorders, such as Parkinson’s disease, impact men and women differently. For example, men are twice as likely to develop PD compared to women.
• Researching sex differences at the level of the norpinephrine system has the potential to discover why the intensity of symptoms, prognosis, time of onset, and more vary between men and women.
• Future studies should focus on additional molecular differences between men and women at the level of the central nervous system and translate the findings to create patient-centered treatment plans.
• Additionally, understanding how hormonal and neurotransmitter systems are influencing sex differences can allow medical personnel and pharmaceutical companies to make educated decisions regarding therapeutic drugs.

References


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