Anatomical and Sex Differences in the Expression of Calcitonin Gene-Related Peptide within the Norepinephrine System

Norepinephrine (NE) is a neurotransmitter that has important functions in both the peripheral (PNS) and central (CNS) nervous systems. In the PNS, NE raises heart rate and blood pressure which is beneficial for the fight-or-flight response, but chronic activation can lead to hypertension and cardiomyocyte apoptosis. Calcitonin gene-related peptide (CGRP) has been shown to mitigate NE-induced apoptosis through vasodilation, illustrating an antagonistic PNS relationship. In the CNS, NE modulates the stress response, mostly through the locus coeruleus (LC), where CGRP has been shown to be expressed. Both CGRP and NE contribute to the onset of migraines via the trigeminovascular system, though this interaction has not been extensively studied. Migraines and stress-related psychiatric disorders are both more prevalent in females, suggesting the possibility of molecular sex differences in the NE and CGRP systems. We used immunohistochemistry to map the expression of CGRP across the NE system to investigate anatomical and sex differences and fill this knowledge gap. Our results showed CGRP is differentially expressed across the NE system with the highest expression in the LC and no expression in A5, A1, or A2. However, our study did not identify significant sex differences which did not support our hypothesis. Although our study did not show significant sex differences in CGRP expression, higher prevalence of migraines and stress-related psychiatric disorders illustrate the importance of investigating molecular sex differences in the interaction of these two systems for the development of sex-specific therapeutic treatments.