Regulation of Glial Cell-Line Derived Neurotrophic Factor in Cardiac Muscle

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Proper and functional innervation of the heart by the autonomic nervous system is critical for healthy cardiac function. Inadequate innervation or an imbalance of the two branches of the autonomic nervous system within the heart have been associated with disorders of the heart such as Heart Failure. Glial cell-line derived neurotrophic factor (GDNF) is critical for the maintenance of the autonomic nervous system. Much is known about the functions of GDNF, but little is known about its regulation. Contractile HL-1 cardiomyocytes served as an investigative model of cardiac muscle. The cells were treated with the two main neurotransmitters of the parasympathetic and sympathetic branches of the nervous system, acetylcholine and norepinephrine respectively, to investigate whether autonomic neurons can regulate their own supply of GDNF from target tissue through neurotransmitter release. Calcium entry was also altered in tissue culture to determine if the GDNF expression was related to contractility. Samples were collected and analyzed for GDNF content using Enzyme-Linked Immunosorbant Assay (ELISA). Heart tissue from an exercise study was also analyzed for GDNF content using ELISA and immunohistochemistry. Neurotransmitter release and exercise release were found to affect GDNF production. An understanding of the mechanisms of GDNF production enables future manipulation of unhealthy autonomic innervation to establish healthy autonomic innervation.

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