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Intrinsic cardiac ganglia
The little brain on the heart

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Introduction

The locations of human intrinsic cardiac neurons and the mediastinal nerves that contain axons connecting with such neurons remain poorly understood despite the fact that the anatomy of this nervous system has been the subject of scrutiny for over a century 1-(Francillon)2-(Kuntz,)3-(Davies et al.) 4-(Mitchell) 5-(Robb). Intrinsic cardiac neurons have been reported to be located in small ganglia scattered primarily over the posterior surfaces of the atria 4-(Mitchell,1956), particularly in the posterior atrioventricular groove 6-(Dogiel, 1899)7-(Glomset). Few neurons have been associated with human ventricular tissues 2-(Kuntz,)3-(Davies) 8-(Janes et al.,1986). Recent work has indicated that the mammalian intrinsic cardiac nervous system is widely distributed, possessing a number of different types of neurons.. These neurons interact via a number of synaptic mechanisms to maintain adequate cardiac output . It is not known whether the human heart possesses such a complex nervous system. The full extent of the distribution of intrinsic cardiac neurons on the human heart and the synaptology of the intrinsic cardiac ganglia remains unknown. Because the functional properties of human intrinsic cardiac neural elements are now amenable to investigation 9-(Murphy)10-(Carlson), it is imperative that the locations and connectivity of human cardiac neurons be determined.

The present study was undertaken to identify the full extent of the human intrinsic cardiac nervous system as well as the interrelationships of its ganglia within different cardiac regions. We estimated the relative numbers of ganglia on the human heart and studied the morphology and synaptology of human intrinsic cardiac neurons. In this manner, we sought to provide an overview of the distribution, size, and anatomic relationships of intrinsic cardiac ganglia and to propose a descriptive terminology that identifies their major cardiac sites in order to help locate this nervous system for functional studies in, for instance, the operating theater

Materials and Methods

Tissues were obtained from hearts of 18 adult humans of either sex aged 28–69 years. Six intact human hearts collected at autopsy were used to determine the distribution and organization of intrinsic cardiac ganglia as well as their interconnecting nerves. To supplement the studies on intact hearts, selected right and left atrial tissues with adjoining fat were collected from an additional ten hearts at the time of autopsy. These tissues were used for light microscopic analysis of intrinsic cardiac neurons. All autopsy tissues were stored at 4°C in physiological saline for 1-2 hours before being processed for gross and microscopic analyses. In addition, atrial tissues collected from two human hearts at the time of cardiovascular surgery were processed for electron microscopic analysis.

Results

Gross Anatomy : Intrinsic cardiac ganglia were typically associated with interconnecting nerves that formed ganglionated plexuses. Ganglionated plexuses were consistently identified in five atrial and five ventricular locations.Single neurons or occasional small ganglia were located in other regions between atrial or ventricular muscle fascicles. Ganglia ranged in size from those containing from one to a few neurons to those that contained over 200 neurons. The overall distribution and estimated numbers of ganglia per heart were compiled from complete dissections of six whole hearts. An average of 458 6 43 ganglia of varying dimensions were identified in atrial tissues, and 88 6 7 ganglia were identified in ventricular tissues . By adding the weighted average of the numbers of neurons associated with atrial and ventricular ganglia ,an estimate of over 14,000 neurons in each human heart was obtained.The precise anatomical configuration of each ganglionated plexus varied considerably from specimen to specimen, as did the sizes of ganglia within a region. Many nerves, some of which had relatively large diameters (up to ,0.2 mm), coursed between ganglia in each region, thereby forming loose regional neural networks, i.e., intrinsic cardiac ganglionated plexuses. Interconnecting nerves between ganglia in a ganglionated plexus sometimes formed complete loops, which ranged from less than 2 mm to 1 cm in diameter, particularly in atrial plexuses .There were extensive regions of atrial or ventricular fat where no ganglia were identified. For instance, few neurons

were identified in the bulk of the fat accompanying the major coronary arteries in the atrioventricular groove.

Microscopic Anatomy

Light microscopic anatomy

Most ganglia occurred as swellings along intrinsic cardiac nerves, especially at branch points ,Individual neurons were occasionally identified in isolation along nerves. Some ganglia were estimated to contain more than 200 neurons . Neuronal somata varied in size, with long axes with a mean of 39 µm (610 µm S.D.) and short axes with a mean of 34 µm (67 µm S.D.). The nuclei of intrinsic cardiac neurons were usually located toward the periphery of the cells and contained a prominent nucleolus. Although most intrinsic cardiac neurons were multipolar , visualization on the basis of dendritic staining with methylene blue also suggested the presence of unipolar and bipolar neurons. Without serial section analysis, it was not possible to determine the number of neuronal processes or their distribution.

Electron microscopic anatomy

The capsule of intrinsic cardiac ganglia was thick and was composed of fibroblasts and collagen fibers. In most respects, neurons were typical autonomic neurons with plentiful cytoplasm that contained many organelles ,At the light microscopic level, it was observed that the large nuclei were usually located eccentrically. The cytoplasm of neurons contained Golgi complexes, smooth and rough endoplasmic reticulum, free ribosomes, and numerous mitochondria. Some neurons also contained accumulations of lipofuscin granules, usually near the periphery of the cell . Neuronal perikarya were completely invested by satellite cell sheaths . The neuropil of ganglia was a complex mixture of axons, dendrites, and supporting tissue consisting mainly of collagen fibers. Dendrites were characterized by microtubules, neuro filaments, and small profiles of smooth endoplasmic reticulum interspersed with mitochondria. Occasional multivesicular bodies were visualized in neurons and satellite cells .

Disccusion

The results of the present investigation demonstrate that large numbers of intrinsic cardiac neurons are associated with ganglionated plexuses in human atrial and ventricular tissues, the latter population being considerably larger and more widely distributed than was previously considered. The anatomical delineation of specific atrial and ventricular ganglionated plexuses based on anatomical landmarks provides, for the first time, a classification comparable to that found in other large mammals . Human intrinsic cardiac ganglia are connected with the more cranially located intrathoracic extracardiac ganglia via cardiopulmonary nerves 11-(Janes et al., 1986), which lie adjacent to the superior vena cava, aortic root, and pulmonary artery ,Smaller mediastinal nerves course laterally to join the adjacent thoracic vagosympathetic trunks. Human intrinsic cardiac ganglia and their associated nerves, which are found primarily embedded in epicardial fat, form five atrial and five ventricular ganglionated plexuses .Individual neurons and small ganglia were also found scattered through atrial and ventricular tissues, the latter being located primarily at the base of the heart.

Each human heart was estimated to contain an average of 550 ganglia of various dimensions. Presumably, this is an underestimation of their total number. Direct visualization permitted assessment of the arrangement of ganglia and their assorted connectivity within various ganglionated plexuses. Al- though methylene blue is useful to determine the anatomical connectivity of such ganglia, many small ganglia are not readily identified by this method. Serial sectioning through tissues, particularly fatty tissue, presents difficulties for counting ganglia, because many ganglia are removed from the tissue during sectioning. Human intrinsic cardiac ganglia were found to be up to 2 mm in length, the majority being associated with nerve branch points At least 14,000 neurons are associated with the human heart, which suggests that the human heart contains about twice as many neurons as the canine heart . Ganglia were identified, as previously reported, on the posterior surface of the two atria and in the interatrial septum Although it has been reported that most human atrial neurons are located between the origins of the two vena cavae 13- (King and Coakley, 1958), in the present study, equal numbers of ganglia

were identified on the postero- medial left atrium and on the posterior right atrium .In a classical mitral valve exposure, the posterior right atrial ganglionated plexus would be affected when the interventricular groove is dissected so that the left atrium can be entered. Because significant populations of neurons are located in this ganglionated plexus, the integrity of this part of the intrinsic cardiac nervous system may be jeopardized during such surgery. Where the posterior right atrial and poster medial left atrial ganglionated plexuses unite, they extend into fat located in the posterior interatrial septum. Contrary to the report of King and ,we did not and a large population of neurons adjacent to the termination of the coronary sinus. Rather, the largest collection of human intrinsic cardiac ganglia was located in the posterior right atrial ganglionated plexus, a region that, when it is stimulated electrically, induces relatively consistent cardiac responses (Murphy and Armour, 1992). The relatively large collection of ganglia on the superior aspect of the right atrium would be vulnerable to destruction during the superior approach to the left atrium via the transverse sinus for mitral valve exposure. The posteromedial left atrial ganglionated plexus behind the inferior vena cava root also contains a sizable population of ganglia. This region is frequently incised during exposure of the mitral valve.

Conclusion

The cardiac nervous system is intimately interconnected to whole body function. Multiple populations of autonomic neurons, in constant communication via a host of neurochemicals, function to maintain cardiovascular stability and maximize cardiac efficiency via a complex regulatory hierarchy of nested feedback control loops, organized in three levels of the nervous system: the intrinsic cardiac nervous system, the intrathoracic extrinsic cardiac nervous system, and the central nervous system. It is vital that these complex, redundant interactions be understood not only in order to develop novel therapeutic strategies for the management of various heart conditions, but also to apply psychological principles to such management.

Abstract

the extent and locations of intrinsic cardiac ganglia on the human heart were investigated to facilitate studying their function.The locations and number of major intrinsic cardiac ganglia were determined in six human hearts by means of microdissection following methylene blue staining. Light and electron microscopic analyses were performed on right atrial and cranial medial ventricular ganglia obtained from 12 other human hearts,Collections of ganglia associated with nerves,i.e., ganglionated plexuses, were observed consistently in five atrial and five ventricular regions. Occasional ganglia were located in other atrialand ventricular regions. Atrial ganglionated plexuses were identified on1) the superior surface of the right atrium, 2) the superior surface of the left atrium, 3) the posterior surface of the right atrium, 4) the posteriormedial surface of the left atrium (the latter two fuse medially where they extend anteriorly into the interatrial septum), and 5) the inferior and lateral aspect of the posterior left atrium. Ventricular ganglionated plexuses were located in fat 1) surrounding the aortic root, 2) at the origins of the right and left coronary arteries (the latter extending to the origins of the left anterior descending and circumflex coronary arteries),3) at the origin of the posterior descending coronary artery, 4) adjacent to the origin of the right acute marginal coronary artery, and 5) at the origin of the left obtuse marginal coronary artery.The conclusion The human intrinsic cardiac nervous system is distributed more extensively than was considered previously, most of its ganglia being located on the posterior surfaces of the atria and superior aspect of the ventricles. Each ganglion therein contains a variety of neurons that are associated with complex synaptology.

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