No. 202437

The Role of Cardiac Mitochondrial Quality in the Increased Risk of Cardiac Diseases Due to Excessive Salt Intake

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Summary

Quality of mitochondria plays a vital role in maintaining cellular homeostasis. The author has previously demonstrated that excessive mitochondrial fission in cardiomyocytes, triggered by ischemic stress or environmental electrophiles, contributes to cardiac dysfunction. This abnormal fission is mediated by the formation of a pathological complex between the mitochondrial fission protein Drp1 and the actin-binding protein Filamin. Furthermore, it was revealed that supersulfides which is highly reactive sulfur metabolites, regulate the Drp1-Filamin complex formation. A decrease in supersulfide levels induced by ischemia facilitates the formation of the Drp1-Filamin complex, leading to mitochondrial dysfunction in cardiomyocytes.

While the importance of salt restriction in heart failure patients is well recognized, the specific mechanisms by which high salt intake directly impairs cardiac contraction and relaxation remain unclear. However, morphological abnormalities in cardiac mitochondria have been observed in salt-sensitive hypertensive rats, suggesting a potential link between salt intake and mitochondrial quality impairment.

In this study, the effect of high salt stress on mitochondrial quality and function was investigated, focusing on the regulation of the Drp1-Filamin complex via supersulfide metabolism. Under hypoxia, cardiomyocytes exhibited mitochondrial membrane depolarization, which promoted a catabolic shift from supersulfides to hydrogen sulfide. In contrast, treatment with high-NaCl media induced mitochondrial membrane hyperpolarization, favoring the anabolic conversion from hydrogen sulfide to supersulfides. Similar changes were observed when cells were exposed to sorbitol-containing media with equivalent osmolarity, indicating that hyperosmotic stress was the driving factor.

Interestingly, high-NaCl treatment did not affect the formation of the Drp1-Filamin complex or alter mitochondrial morphology. However, mitochondrial energy production was impaired, suggesting that hyperosmotic stress modulates mitochondrial function through mechanisms distinct from those involved in hypoxic stress. Elucidating these unique pathways of mitochondrial regulation under high-salt conditions remains an important direction for future research.