MthK channels as a function of \([\text{Ca}^{2+}]\) and ion conductance and gating properties of recordings, Li and colleagues analyzed the Observations:

are bound, one per RCK domain, a confor-

tification. Finally, two gating processes

voltage-dependent manner, which implies

Observations: Using single-channel

Significance: Although there are several

Significance: This is the first time that changes in body temperature have been shown to affect lifespan in warm-blooded animals independent of changes in diet. These findings are particularly intriguing given the abundance of evidence that demonstrates increased weight correlates with a shortened lifespan.

Question: What is the molecular/structural basis for the gating properties of the \([\text{Ca}^{2+}]\)-gated \(\text{K}^+\) channel MthK?

Background: MthK is a \([\text{Ca}^{2+}]\)-gated \(\text{K}^+\) channel that contains conserved COOH-terminal ligand-binding domains named RCK (for regulating the conductance of \(K^+\) channels). A functional MthK channel requires eight RCK \([\text{Ca}^{2+}]\) binding domains to form an octameric gating ring on the intracellular side of the pore. Hence, when eight \([\text{Ca}^{2+}]\) ions are bound, one per RCK domain, a conformational change occurs that results in an opening of the pore.

Question: Is the reduction in core body temperature induced by caloric restriction requisite for increasing longevity?

Background: Mammalian temperature homeostasis is regulated by the preoptic area (POA) of the hypothalamus. Thus local or peripheral changes in temperature are sensed by the POA, which coordinately a thermoregulatory response to maintain core body temperature (CBT). Lowering CBT slows the aging process and extends the lifespan of cold-blooded animals. Lifespan extension in warm-blooded animals is achieved by reducing caloric intake, a dietary regimen that also reduces CBT. However, it is not clear whether the caloric restriction alone can increase lifespan or whether the reduction in CBT was a necessary phenomenon.

Observations: Based on the knowledge that insertion of heat probes into the POA causes a reduction in body temperature, Conti et al. hypothesized correctly that inducing the production of large quantities of uncoupling protein 2 near the preoptic area would produce heat, which would diffuse to other brain structures, including the preoptic area. In turn, the extra heat induced a continuous reduction of the CBT of the mice, lowering it 0.3–0.5°C. This lowered CBT resulted in significantly longer median lifespans. Interestingly, this effect was more pronounced in females, whose median lifespan was extended about 20% vs. 12% in males. Although the transgenic mice showed no change in caloric intake or physical activity, they did gain weight.

Significance: These results suggest that \(K^+\) channels, under normal low \(K^+\) conditions, prevent \(Na^+\) conduction because \(Na^+\) favors the nonconductive conformation, not because \(Na^+\) cannot diffuse across the conductive filter. In addition, another fundamental aspect of the channel borne out by these studies is that \(K^+\) prevents \(Na^+\) conduction because the multiple binding sites in the conductive filter preferentially bind \(K^+\) over \(Na^+\). Given the near ubiquitous expression of \(K^+\) channels, these results may have widespread implications for understanding several disease states.


Question: Can acute exposure to antioxidants prevent the cardiovascular effects of diving?

Background: Although recreational diving has become a popular pastime for millions of people, it is associated with environmental stresses that affect hemodynamics and cardiovascular function. For example, field scuba diving causes an increase in pulmonary artery pressure and endothelial dysfunction. Obad et al. previously demonstrated that chronic (4 weeks) exposure to the antioxidants vitamin C and E reversed the acute endothelial dysfunction observed after diving. Here, they sought to determine whether acute exposure to antioxidants would attenuate the negative effects of diving on cardiovascular and endothelial function.

Observations: Obad and colleagues demonstrated that scuba diving, at depths and durations similar to those enjoyed by recreational divers, can cause modest reductions in cardiovascular and blood vessel function for several days after the dive. However, predive ingestion of vitamins C (2 g) and E (400 IU) partially prevented some of the negative effects of the dive, suggesting that diving-associated oxidative stress contributed to the changes.

Significance: Although the changes in cardiovascular and blood vessel function were not a threat to the health of the divers, this study raises the possibility that routine predive supplementation with antioxidant vitamins would be beneficial. This study is likely to be of interest to recreational divers and also to those involved in military and industrial diving.

Question: What role, if any, do cardiac neural crest cells play in the development of the His bundle?

Background: The cardiac conduction system involves the generation of an electrical impulse from the sinoatrial node (SA node) that is conducted by the atrioventricular node (AV node) to the bundle of His, which transmits the impulses to the Purkinje fibers that innervate the ventricles and cause the heart to contract. One essential feature of the His-Purkinje conduction system is that it is electrically isolated from surrounding tissues to prevent dissipation of the excitatory impulse. Although an association has been made between the development of the cardiac conduction system and neural crest cells, whether neural crest cells affect the differentiation and/or function of the bundle of His was not known.

Observations: Gurjarpadhye et al. sought to determine whether ablation of the cardiac neural crest cells would affect the cardiac conduction system. They provide evidence consistent with a role of neural crest cells in the development of the His bundle. In fact, they found that neural crest ablation resulted in His bundle cells maintaining electrical connections with surrounding myocardium. They also noted the requirement for neural crest cells in the development of insulation in cardiac conduction bundles and nerves. Moreover, His bundles from ablated embryos did not undergo the normal remodeling associated with development. Finally, whereas the His bundle diameter thinned in control hearts, ablation resulted in His bundle diameters that did not undergo such thinning.

Significance: These data suggest that the cardiac neural crest plays a role in the differentiation, specialization, and electrical isolation of the His-Purkinje conduction system.

Perhaps these findings will aid in elucidating the pathology of some cardiac diseases, such as infrahisian heart block, which is a dysfunction in the electrical conduction system of the bundle of His.

Question: Is neonatal diuretic treatment predictive of sodium intake in children?

Background: The amount of sodium individuals consume varies widely. The reasons for the wide variations in sodium consumption are unknown, but because long-term sodium intake is a key marker for obesity, it is an important question. Previous work by this group found that children who received neonatal diuretic therapy excreted more sodium than controls, which suggests they consumed more sodium. Thus, in the current study, they hypothesized that dietary sodium consumption in children would be predicted by neonatal diuretic treatment.

Observations: Shirazki et al. examined the sodium appetite of children (ages 8–15 yr) born prematurely and whether they received neonatal diuretic treatment during their first postnatal month. They also assessed serum sodium measurements of the infant’s as an index of sodium loss. In contrast to their hypothesis, dietary sodium intake in children was predicted by neonatal lowest serum sodium, not neonatal diuretic treatment. This was true of two ethnic groups and both boys and girls. Finally, they found that the most severe cases of low-sodium blood serum was found in children who consumed significantly more sodium per day and weighed 30% more than their peers.

Significance: This study suggests that long-term intake of sodium is impacted by neonatal events. In infants, low-sodium blood serum, not neonatal diuretic treatment, gestational age, or birthweight, was predictive of an increase in sodium consumption in childhood. The relationship between...
Background: ED is a common complication of diabetes; however, the pathophysiological mechanisms that underlie this dysfunction are unknown. Sildenafil (Viagra) works peripherally and is effective 50% of the time in diabetic patients, which implies another mechanism may underlie the dysfunction in some patients. Centrally, nitric oxide (NO) within the paraventricular nucleus (PVN) is putatively synthesized in response to N-methyl-D-aspartic acid (NMDA) receptor activation to mediate penile erection. Thus the possibility that NMDA/NO-induced penile erection was impaired in the PVN was explored in diabetic rats.

Observations: The authors compared induced erection via the PVN in control and diabetic male rats. The results of the study showed that NMDA-induced erections were blunted in the diabetic rats and that sodium nitroprusside (an NO donor)-induced responses were also significantly blunted. In addition, the expression of the neuronal NO synthase (nNOS) isoform was dramatically reduced in the PVN region from diabetic rats but not in two other adjacent forebrain regions. Finally, the erectile response was recovered by over expression of nNOS by gene transfer using an adenoviral transfection into the PVN.

Significance: This study addresses a very important and under-investigated area of research: the role of the central nervous system in erection. These results support the hypothesis that a central NO mechanism within the PVN may contribute to the ED observed in diabetes. Examining the mechanism of diabetes-induced ED is very topical given the alarming rate at which diabetes is increasing.