Sensing acid in the brain

A study performed by Cakir et al. finds that acid-sensing ion channels, including calcium, sodium, lead, and zinc have varying effects on the excitability of stellate cells in the cochlear nucleus.

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Introduction

Calcium toxicity is currently the most promising cause of ischemic brain injuries, and the resulting acidity may be the method of damage. Acid-sensing ion channels (ASICs) can be permeable to calcium, and when blocked can prevent ischemic brain injuries.[1] Stellate cells have been discovered to have several isoforms of ASICs, but their properties are still largely unknown. In a paper published last year by the Journal of Comparative Physiology, researchers Cakir, Yildirim, Buran, Onalan and Bal look at the excitability of stellate neurons due to the acid-sensing ion channels (and their ionic permeability) in the cochlear nucleus.[10] The cochlear nucleus is the relay station between the auditory nerve and the higher auditory processing centers of the brain.[2] Stellate cells have been identified as important to speech comprehension and sound localization.[2]

Background

Stellate cells–which can be subdivided into T and D type stellate cells– are one of three main cells found in the cochlear nucleus, and they are one of six pathways to the inferior colliculus.[3,4] Acid sensing ion channels (ASIC) are voltage independent and proton dependent, and have been found in stellate cells.[5] Acid sensing ion channels are channels that create propagations based on the surrounding pH, and these channels were previously associated with taste, nociception, etc. ASICs are cation specific, therefore it is important to understand which cations it responds to for further determining function of the stellate cell.[5] Out of the three main cells in the cochlear nucleus, stellate cells are the only ones who respond to repeated signals in order to create its own signal. Acid sensing ion channels have different subunits and depending on their makeup, they have different functions and signals that it responds to.

Methods

This study took DNA from the cochlear nucleus and using a process called Real Time Polymerase Chain Reaction, they were able to increase the amount of DNA so that it was easier to manipulate. Then they took the DNA strands that make up the acid sensing channel subunits so that they would bind to the place on the DNA that was taken from the cochlear nucleus to see if there was a match to confirm the presence of the acid sensing ion channels. After they confirmed the presence of those subunits, they moved to see how these subunits worked in the brain by using a patch clamp technique. The patch clamp technique is when the researcher identifies a neuron in the living brain (in this case a mouse) and they use a small pipette to give small doses of ions or electricity to that neuron to see how it reacts and whether or not it sends a signal.

Results

The paper looked at various ions to see whether or not their presence would increase or decrease the amplitude of the signals that the stellate cells produce in response to the ions. Some of these acid sensing ion channels were found to respond to sodium molecules as a signal while others respond to calcium, while others only respond to a mixture of sodium and calcium. Most of the subunits activated around the pH of 7 and continued as the pH became more acidic. Throughout development, they are found to be present and don't appear to go away, which seems to mean that they aren't important to a certain developmental time period. Lead and zinc were also looked at. Lead decreased the signaling of stellate cells while zinc increased it when there was a high concentration of zinc, but when there was only a small amount it tended to decrease the amount of signaling.[8]

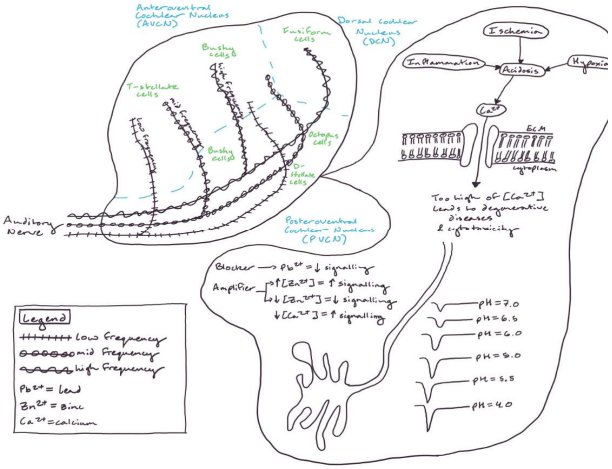

Figure 1. Role of acid sensing ion channels on excitability of stellate cells found in the cochlear nucleus.[6,7]

Significance

The importance of these findings is in related to diseases such as ischemic stroke, epilepsy and multiple sclerosis that tend to be correlated with acidic pH. A change in pH is often associated with inflammation or by proinflammatory factors. If there is a low pH chronically, then stellate cells would continue to fire and this overactive signaling could lead to toxicity. In animals without acid sensing ion channels, there is a lowered fear response to predators, and therefore increase numbers of ASICs may be involved in anxiety disorders.[9] As far as hearing loss, stellate cells weren't correlated with direct hearing loss but with the sensitivity of hearing. This paper identifies acid sensing ion channels and their diversity in form and cationic permeability. Future research should look at the correlation between the proportions of these acid sensing ion channels found within stellate cells and the role of stellate cells in converting primary auditory firing to chopper patterns, which appears to be another large area of research.[3]

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