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Acid-sensing ion channels: trafficking and synaptic function.

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Extracellular acidification occurs in the brain with elevated neural activity, increased metabolism, and neuronal injury. This reduction in pH can have profound effects on brain function because pH regulates essentially every single biochemical reaction. Therefore, it is not surprising to see that Nature evolves a family of proteins, the acid-sensing ion channels (ASICs), to sense extracellular pH reduction. ASICs are proton-gated cation channels that are mainly expressed in the nervous system. In recent years, a growing body of literature has shown that acidosis, through activating ASICs, contributes to multiple diseases, including ischemia, multiple sclerosis, and seizures. In addition, ASICs play a key role in fear and anxiety related psychiatric disorders. Several recent reviews have summarized the importance and therapeutic potential of ASICs in neurological diseases, as well as the structure-function relationship of ASICs. However, there is little focused coverage on either the basic biology of ASICs or their contribution to neural plasticity. This review will center on these topics, with an emphasis on the synaptic role of ASICs and molecular mechanisms regulating the spatial distribution and function of these ion channels.