

海马神经细胞胆固醇含量降低对其电压依赖钾电流的上调作用

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胆固醇普遍存在于细胞膜中,其含量在细胞增殖、生长及各种疾病条件下会发生改变,这暗示胆固醇对细胞功能的调节起着重要的作用。运用全细胞膜片钳技术研究了胆固醇含量变化对海马神经细胞电压依赖钾电流的影响。实验观察到神经细胞经胆固醇去除剂 β -甲基环化糊精(M β CD)处理后,胆固醇含量的减少促进了延迟整流钾电流IK的增加,且延缓了瞬间失活钾电流IA的失活。更进一步,延迟整流钾电流IK和瞬间失活钾电流IA分别经TEA和4-AP阻断后,M β CD对两种电流成分的影响显著降低。这一结果进一步表明胆固醇去除剂对电压依赖钾电流的上调是通过作用于IK和IA电流而共同实现的。基于电压依赖钾通道在神经细胞功能中的重要作用,实验结果暗示神经细胞胆固醇含量变化可对神经细胞的兴奋性起调节作用。

Cholesterol depletion up-regulates voltage-dependent K⁺ current in rat hippocampal neurons

Cholesterol is ubiquitous in cell membranes and its content changes during development, aging or in various diseases, this means that it plays an important role in modulating cell functions. This study investigated whether changes in cholesterol content could modulate activity of the voltage-dependent K⁺ (K_v) current in rat hippocampal neurons by using whole cell patch clamp technique. Acutely depletion of membrane cholesterol by exposing the cells to methyl-beta-cyclodextrin (M β CD), a cholesterol-sequestering molecule, resulted in an enhancement of IK (delayed rectifier potassium current) and delaying the inactivation of IA (transient outward potassium current). Furthermore, cholesterol depletion almost had no effect on IK and IA current after treatment with TEA and 4-AP on the cells, respectively, indicating that the effect of membrane cholesterol on up-regulation of the K_v current was due to the activation of both IK and IA currents. In view of important roles of IK and IA currents in the neuronal functions, these results suggest that cholesterol may play a regulatory role in the neuronal excitability.

关键词

胆固醇(Cholesterol); Hippocampal neuron(海马神经细胞); β -甲基环化糊精(Methyl- β -cyclodextrin); 电压依赖钾通道(Voltage-dependent potassium channel)