離體天竺鼠氣管冷卻降溫反應機轉之研究

Studies on the mechanisms of cooling induced responses in isolated guinea-pig trachea

中文摘要

運動後引起的氣喘與溫度有關，但其機轉至今未明。本實驗在探討冷卻作用對離體天竺鼠氣管的影響。我們發現冷卻作用會使氣管產生短暫微小的收縮反應接連著持續性鬆弛反應。而 histamine(1-300u M)，serotonin(0.1-30u M)及 ryanodine(0.1-30uM)會依劑量增加而加強冷卻誘發鬆弛反應。想反地，carbachol(0.1-10uM)會抑制冷卻誘發鬆弛反應；甚至於在劑量大於等於 10uM 時反轉成收縮反應。而 ryanodine 預處理能抑制 carbachol 存在下的冷卻收縮反應。在 cyclooxygenase 的抑制劑 indomethacin(10uM)存在下，serototin 及低劑量 carbachol 的冷卻誘發鬆弛反應完全被返轉成收縮反應；Histamine 在低劑量也是相同反應，但在高劑量時又恢復冷卻鬆弛反應。想反地，ryanodine 卻能抑制此一冷卻收縮反應。另外，在 lipoxygenase 的抑制劑 NDGA(25uM)存在下的結果與 indomethacin 類似。

Carbachol 在最大劑量的情況下，依然可見冷卻加強收縮反應。此一收縮反應能被 ryanodine(30uM)預處理能所抑制。Sodium pump 抑制劑 ouabain(10uM)能抑制天竺鼠氣管的冷卻誘發收縮反應；但卻不能抑制 carbachol(30uM)存在下的冷卻收縮反應。而且 nifedipine 及 CPA 也無法抑制 carbachol 的冷卻收縮反應。

總而言之，根據我們的實驗結果推斷:1)離體天竺鼠冷卻降溫反應由一個收縮相及一個鬆弛相所組成。2)冷卻鬆弛反應與內生性 arachidonic acid 代謝物有關。3)冷卻誘發細胞內鈣離子流出可能與 ryanodine 受體有關。

英文摘要

It was reported that exercise-induced asthma is associated with the temperature reduction of the airway smooth muscle. However, the precise mechanisms which may involve are poorly understood. We studied the effect of cooling on isolated guinea-pig trachea. In our results, cooling induced a small and transient contraction followed by a sustained relaxation. In addition, histamine(1-300uM), serotonin(0.1-30uM)and ryanodine(0.1-30uM) potentiated cooling-induced relaxation in a dose dependent manner. Conversely, carbachol inhibited the cooling induced relaxation to contraction at high concentraction(>10uM). Cooling-in-duced contraction under carbachol high concentration were abolished by ryanodine pretreatment.

In the presence of indomethacin, cooling-induced relaxations response to serotonin and low dose carbachol were reversed to contraction completely. Similar results were observed at low dose histamine, however, the relaxation responses were restored at

high concentration. In contrast, cooling-induced contractions in previous statements were abolished by ryanodine pretreatment.

Cooling-indued contraction can be inhibited by ouabain, a potent inhibitor of sodium pump, pretreatment. However, ouabain, nifedipine and CPA did nnot affect cooling-induced contraction under carbachol developed tension.

In conclusion, we have presented data 1)demonstrating that the cooling responses are composed by a contraction phase and relaxation phase in isolated guinea-pig trachea, 2)indicating that cooling-induced relaxation is associated with endogenous arachidonic acid metabolites, 3)raising the possibility that cooling induced internal calcium release may involve in ryanodine receptors