Ultra-low dose naloxone suppresses microglia activation via HSP90 alpha fragmentation

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ABSTRACT

Background/Purpose: As we known, long-term morphine treatment leads to tolerance. We previously demonstrated that ultra-low dose naloxone restores the antinociceptive effect of morphine in morphine-tolerant rats via suppressing microglia activation. However, microglia constitute only 5-12% of all cells in the central nervous system (CNS), which leads to some impairment role of microglia been ignored. Therefore, in the present study, we further investigated the effect of ultra-low dose naloxone in morphine-induced activated microglia BV2 cells.

Methods: BV2 mouse microglia cells were treated with DMEM or ultra-low dose (1 nM) naloxone 30 minutes before addition of medium or 1 μM morphine and incubation for 2 h at 37ºC in a 5% CO2 atmosphere. The cells were then collected and performed analysis.

Results: Morphine not only significantly induced morphological changes of cultured BV2 cells, but also induced heat shock protein 90 alpha (HSP90α) fragmentation. All of these changes were abolishable by pre-treatment with ultra-low dose naloxone.

Conclusion: We demonstrated a novel phenomenon that ultra-low dose naloxone inhibits morphine-induced microglia activation by preventing HSP90α fragmentation. Our results broaden the molecular basis of morphine-induced microglia activation.

Keywords: morphine-tolerance, HSP90, neuropathy, cleavage, membrane ruffling.

REFERENCES

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