ABSTRACT

Aim of Investigation:
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 suppresses microglia activation. We further investigated that, ultra-low dose naloxone suppressed neuro-inflammation through prevention of heat shock protein 90 (HSP90) cleavage in morphine-induced activated microglia EOC13.31 cells. We found that, morphine enhanced EOC13.31 cell activation and induced HSP90 fragmentation, and the fragments of HSP90 cluster near the Golgi. We suggest that, Golgi perhaps play an important role in morphine tolerance development.

Methods:
EOC13.31 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 perform followed analysis.

Results:
Our results showed that morphine enhanced microglia activation and migration, induced HSP90 fragmentation and histone deacetylase 6 (HDAC6) expression. Moreover, morphine-induced α-tubulin deacetylation and HSP90 fragmentation were HDAC6-dependent. Pretreatment with naloxone (1 nM) not only inhibited morphine-evoked microglia activation, but also prevented HSP90 fragmentation and gather around Golgi by inhibiting HDAC6 expression.

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

Keywords: Golgi, Morphine Tolerance, and cytoskeleten

REFERENCES

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