

Propofol Inhibits LPS-Induced BV-2 Microglia Cells Activation via Inhibition of TLR4: Possible Involvement of GSK-3 β

BACKGROUND: Microglia is as an immune cell in CNS and to be able to produce many inflammatory mediators in response to stressors ,so that play a critical role in the neuroinflammatory processes. Inflammation is a crossover in the pathogenesis of the chronic neurodegenerative diseases, such as Alzheimer's Disease, Parkinson's disease. Toll-like receptors (TLRs), especially TLR4 in the microglia is a important signaling pathway for inflammation response. Lipopolysaccharide (LPS) can activate microglia, which via toll-like receptor 4 (TLR4), and stimulate the expression of inflammatory cytokines. Also, glycogen synthase kinase-3 β (GSK-3 β) can modulate the inflammatory responses and tilt the balance in favor of pro-versus anti-inflammatory cytokines. Propofol, a well-known anesthetic, has been reported to inhibit LPS-induced inflammation response,such as in macrophagocyte. The aim of our study was to investigate the effect of propofol on LPS-induced inflammation in BV-2 microglia cells, which has been widely used in vitro experiments, and explore whether this effect is related to TLR4 and GSK-3 β .

METHODS: Cells were randomly divided into four groups by using random number table: C group(Control group), LPS group, Propofol group and LPS+ Propofol group. The concentration of LPS and propofol were 1 μ g/mL and 30 μ M, respectively. Cell viability was measured using 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay. Interleukin (IL)-1 β and tumors necrosis factor- α (TNF- α) released in culture medium were examined by enzyme-linked immunosorbent assay (ELISA). TLR4 mRNA expression was analyzed by reverse-transcription (RT) and real-time polymerase chain reaction (PCR). Protein expression of TLR4, p-GSK-3 β and total GSK-3 β were analyzed by western blotting. Statistical analysis was performed with GraphPad Prism statistical procedures. One-way analysis of variance was used followed by Dennett's t multiple comparison test. A P-value <0.05 was considered statistically significant.

RESULTS: Compared with group C, the production of IL-1 β , TNF- α , TLR4 and phosphorylation of GSK-3 β in the LPS group were significantly increased ($P<0.05$). Meantime, content of IL-1 β , TNF- α and TLR4 expression were significantly decreased, whereas phosphorylation of GSK-3 β increased in LPS+Propofol group compared with LPS group(See:Table 1/Figure 1). No significant differences were detected in the content of above targets between group C and group Propofol ($P>0.05$).

CONCLUSIONS: Our results demonstrate that 30 μ M propofol pretreatment reduces the release of inflammatory cytokines induced by LPS in BV-2 microglia cells. Propofol not only increase phosphorylation of GSK-3 β ,but also inhibits TLR4 expression. It suggests thatTLR4 and GSK-3 β may be the important cellular mediators involved in the anti-inflammation effects of propofol on LPS-induced neuroinflammation in microglia.

KEYWORDS: Glycogen synthase kinase 3 beta; Inflammation; Lipopolysaccharide; Propofol; Toll-like receptor

Figure 1:

Table 1. The expression level of IL-1 β and TNF- α in BV-2 microglia cells. [n=8, M(P25~P75), pg/mL]

target	C	LPS	propofol	LPS+propofol
IL-1 β	200(151~368.5)	1600(1314~2210)*	230(152~397.5)	708(536~828)*#
TNF- α	215(148~300.5)	1180(946~1202)*	310(176.5~317.5)	500(319.5~554)*#

Statistically significant from C group ($P<0.05$). #Statistically significant from LPS group (# $P<0.05$).

Figure 2

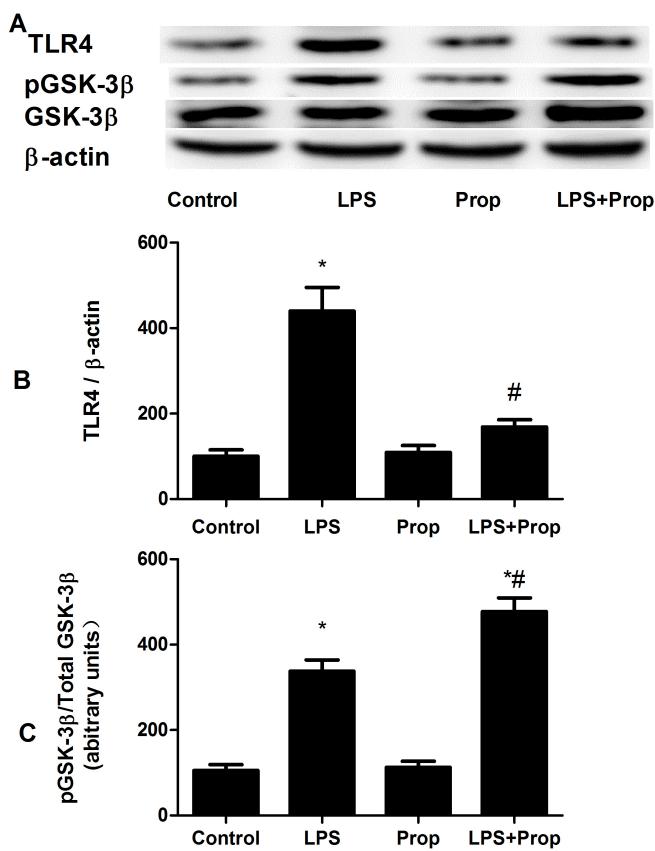


Figure 1. Effects of propofol (Prop) on TLR4 and p-GSK-3 β protein expression induced by LPS in BV-2 microglia cells. *Statistically significant from C group (*P<0.05). #Statistically significant from LPS group (#P< 0.05).