Propofol induces apoptosis and inhibits the proliferation of rat embryonic neural stem cells via gamma-aminobutyric acid type A receptor

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ABSTRACT. We investigated the effect of propofol on the proliferation and viability of rat embryonic neural stem cells (rENSCs) and the potential mechanisms involved. rENSCs were isolated and cultured *in vitro* and treated with 1, 10, or 50 μM propofol, while the control group was treated with 0.1 μM dimethyl sulfoxide. The effect of propofol on the proliferation and viability of rENSCs was examined by proliferation and apoptosis assays. Real-time polymerase chain reaction was employed to analyze the mRNA expression of checkpoint kinase 1 (Chk1) and p53 in rENSCs exposed to propofol. Immunoprecipitation assay and western blotting analysis were performed to analyze the effect of propofol on Chk1 and p53 activity. The gamma-aminobutyric acid type A ($GABA_A$) receptor antagonist securinine was added to the rENSCs before being treated with propofol to investigate the role of the $GABA_A$ receptor in propofol-triggered effects on rENSCs. rENSCs specifically expressing nestin protein were successfully isolated and cultured for experiments. The inhibitory effect of propofol on rENSCs increased dose-

dependently. The percentage of apoptotic cells increased to 11.7% and the activity of Chk1 and p53 enhanced after treatment with 50 μM propofol. However, addition of securinine abrogated propofol-induced apoptosis and activation of Chk1. The $GABA_A$ receptor mediates propofol-induced apoptosis and proliferation inhibition of rENSCs, possibly by modulating the Chk1/p53 signaling pathway.

Key words: Apoptosis; Gamma-aminobutyric acid type A receptor; p53; Checkpoint kinase 1; Cell proliferation; Propofol

