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Amnesia induced by sevoflurane and halothane anaesthesia coexists with a 5-HT_{1A} receptor dysfunction in the rat brain

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Background: Inhaled anaesthetics may cause postoperative amnesia (Rörtgen et al., 2010). 5-HT_{1A} receptors have been implicated in learning and memory (Ogren et al., 2008).

Aim: To assess 5-HT_{1A} receptors contribution to memory impairment after sevoflurane (SEVO) and halothane (HALO) inhaled-anaesthesia.

Methods: Experimental procedures followed the European Communities Council Directives and were approved by local authorities. Male Sprague-Dawley rats (N=30, 6 months old, weight 246±21 g, Charles River-Spain) were randomized into 5 groups (6 rats/group): sham, SEVO group received 1 minimum alveolar concentration (MAC) (2% inspired concentration SEVO in oxygen/1 h, Abbott Lab), HALO group received 1 MAC (2% inspired concentration HALO in oxygen/1 h, Abbott Lab), SEVO-WAY group received SEVO+WAY 100635 (Selleckchem) (0.3 mg/kg s.c. before anaesthesia, and HALO-WAY group received HALO+WAY 100635 (same doses). Anaesthesia was done during 1 h. The 8 arms radial labyrinth test (Egashira et al., 2006) was done 24 h post-anaesthesia to quantify the memory function. The open-field test was used to quantify the locomotor activity. The 5-HT_{1A} receptors were characterized by quantitative receptor autoradiography with the 5-HT_{1A} selective agonist ^{3}H-8OH-DPAT (0.005-10 nM, Amersham-UK) by saturation experiment in limbic areas and dorsal raphe nuclei (coronal sections at Bregma -3.6 mm and -7.3 mm, respectively) (Sato et al., 2008). Results are expressed as mean±sem and were compared by Student t test and ANOVA test followed by Bonferroni post-test.

Results: Labyrinth test data showed a reduction of the retrograde memory in SEVO and HALO groups (SEVO/HALO percentage of change vs. Sham): i) Increased reaction time in first accurate choice (+45.6%/+56.8%) and first 8 accurate choices (+61.5%,+72.98%); ii) Reduced ability to remember the food location in the labyrinth arms: increased number of completed error choices (+71.5%/+96.1%); reduced number of completed correct choices (-35.4%/-46.1%); and reduced number of completed correct choices realized in the first 8 choices (-31.2%/-43.05%)($p<0.05$). WAY 100635 neutralized the memory deficit caused by SEVO and HALO. SEVO and HALO groups` reduced response in the labyrinth test do not seem to be linked to a possible locomotor function deficit, thus both groups locomotor activity was not affected in the open-field test. Inhaled anaesthetics reduced dorsal raphe 5-HT_{1A} receptors affinity (K_D): sham 2.4±0.20 nM < SEVO 6.5±0.82 nM = HALO 7.8±0.66 nM ($p<0.05$); and increased limbic areas 5-HT_{1A} receptors affinity (K_D): hippocampus CA1: sham 5.1±0.75 nM > SEVO 0.50±0.21 nM = HALO 0.68±0.10 nM; fronto-parietal cortex: sham 3.9±0.3 nM > SEVO 1.9±0.15 nM = HALO 1.31±0.12 nM; and amygdala: sham 4.8±0.45 nM > SEVO 1.78±0.19 nM = HALO 2.91±0.21 nM; ($p<0.05$). WAY 100635 neutralized changes of 5-HT_{1A} receptors affinity caused by SEVO and HALO. No changes in 5-HT_{1A} receptors density were detected.

Conclusion: Memory deficit observed after halothane and sevoflurane anaesthesia coexists with a reduced function of dorsal raphe 5-HT_{1A} receptors and an increased function of limbic areas 5-HT_{1A} receptors.

References: Rörtgen et al. (2010) *Br J Anaesth*, **104**(2), 167-74.

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