Morphine decreases 5-HT2A receptor binding measured with SPECT in the canine frontal cortex.

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Both the serotonergic and the opioid neurotransmitter systems play an important role in mood disorders and pain regulation. Electrophysiological and behavioral studies have previously demonstrated a physiological interaction between the serotonin-2A and μ-opioid receptors.

Aim: to investigate the influence of a single injection of morphine on cerebral serotonin-2A receptor (5-HT2A) binding in dogs with ^{123}I-5I-R91150, a selective 5-HT2A receptor radioligand, and SPECT.

Material and Methods: 5-HT2A binding was estimated with (M) and without (control) morphine pretreatment (0.5 mg kg^{-1} intravenously (IV), 30 minutes prior radioligand injection) in eight 5-year-old female beagles. Scans were carried out with a triple head gamma camera (Triad, Trionix) 90 minutes after ^{123}I-5I-R91150 injection (15.07 ± 2.69 MBq kg^{-1} IV). Dogs were premedicated with dexmedetomidine and anesthesia was induced with propofol and maintained with isoflurane in oxygen. Semiquantification, with the cerebellum (a region void of 5-HT2A receptors) as a reference region, was performed to calculate the 5-HT2A receptor binding index (BI) in the frontal, parietal, temporal and occipital cortex and the subcortical region. Data were analyzed by mixed-model ANOVA. Significance was set at $p < 0.05$.

Results: A significantly decreased 5-HT2A receptor BI was found after morphine administration in the right and left frontal cortices (resp. 1.41 ± 0.06 and 1.44 ± 0.08) compared to the blank scan (resp. 1.53 ± 0.10 and 1.55 ± 0.11) with $p = 0.012$ and 0.040 resp. No significant differences were noted for the other regions.

Conclusion: morphine administration decreases frontocortical 5-HT2A receptor availability. This confirms an interaction between the serotonergic and the opioid neurotransmitter system. Whether the decreased radioligand binding is the consequence of decreased receptor density due to downregulation/internalization or the result of indirect actions, such as increased release of endogenous serotonin, remains to be elucidated.

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