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Investigation of the properties of ketamine on rat Mu opioid receptors expressed in *Xenopus* frog oocytes

Ketamine is an intravenous anesthetic agent and analgesic that has been shown to interact with the mu opioid receptor. Since reports differ in showing that ketamine is either an agonist or antagonist at the mu opioid receptor, we tried to find conditions under which we could demonstrate both of these properties of ketamine. Rat opioid receptors and potassium channels were expressed in *Xenopus* frog oocytes and different concentrations of ketamine were tested for agonist and antagonist effects on these receptors. We found that ketamine acts as an agonist at the mu opioid receptor. However, it acts as an antagonist when either the endogenous opioid, DAMGO, or the clinically used analgesic drug, morphine, was present. Both the agonist and antagonist effects were observed at concentrations of ketamine at or below those measured clinically in the plasma during anesthesia. The desensitizations of DAMGO and morphine activations of the mu opioid receptors were studied in the presence and absence of ketamine. It was found that regardless of the combination, all of the desensitization rates were similar. Naloxone, an antagonist at the mu opioid receptor, blocked the ketamine, morphine, and DAMGO responses thus providing additional evidence that ketamine activates this receptor. These results suggest that ketamine interacts with the opioid receptor and this interaction may partially explain its anesthetic and analgesic effects.