# Effects of Clinically Used Sedative/Anesthetic Drugs on Memory for Aversive Experiences in Rats

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The occurrence of traumatic experiences associated with perioperative awareness or Intensive Care Unit (ICU) treatment could result in stress-related disorders such as chronic anxiety, depression or posttraumatic stress disorder (PTSD) (Schelling et al., 2003; Kapfhammer et al., 2004). PTSD is characterized by an excessive retrieval of traumatic memories leading to an over-consolidation process, thus cementing the traumatic memory trace, and retaining its vividness and power to evoke distress for decades or even a lifetime (De Quervain et al., 2009). As patients often have experienced stressful events such as preoperative fear and anxiety, car accidents, myocardial infarctions or acute respiratory distress shortly before induction of general anaesthesia or sedation, it is crucial to investigate the effects of this anaesthetic and sedative agents when administered shortly after the acquisition of new information, a time window when the memory trace is consolidated into stable long-term memory. We have demonstrated that the anesthetic agent propofol enhances fear memory consolidation *via* interaction with the endocannabinoid system (Hauer et al., 2011). In the present study we investigated the effects of clinically used sedative/anesthetic drugs on memory consolidation for emotionally arousing experiences. In particular, we tested the effects of (a) ketamine, a drug widely administered in emergency care and often correlated with sustained PTSD symptomatology; (b) ketamine + midazolam, the benzodiazepine midazolam is often combined with a small-dose of ketamine for sedation to attenuate the cardiostimulatory response of ketamine and to prevent unpleasant emergence reactions; (c) dexmedetomidine, increasingly used as an anesthetic adjunct to reduce the rate of delirium in a variety of clinical settings; (d) the volatile agents isoflurane or sevoflurane used for inhalation anaesthesia in laboratory rodents and humans, respectively. To this aim different groups of male adult Sprague-Dawley rats were trained in an inhibitory avoidance task and injected intraperitoneally with the sedative/anesthetic agents immediately post-training in order to selectively modulate the early phases of memory consolidation. Memory retention was test 48hr later. We found that ketamine either alone or co-administered with midazolam enhanced memory retention of the inhibitory avoidance training while dexmedetomidine dose-dependently impaired it. Posttraining administration of both isoflurane and sevoflurane impaired aversive memory consolidation. Our findings from animal experiments help to understand the neural underpinnings of anaesthetic/sedative effects on memory consolidation of aversive experiences, providing testable clinical hypotheses for clinical studies aimed at evaluating which of these drugs can be used in individuals during the aftermath of an acute traumatic event.

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