

**PD-32. REMIFENTANIL NEUROTOXICITY: NEUROPATHOLOGIC EFFECTS IN RATS AND NEUROMETABOLIC EFFECTS IN HUMANS**

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$\mu$  opioids in clinically relevant high doses to rats have been demonstrated to produce limbic system hypermetabolism and histopathology. This study extends these observations, in both rats and humans, for the short acting drug remifentanil, which allows more precise control and assessment of the effects of the opioid exposure. Two series of experiments were done: one in rats for neuropathologic effects and the second for neurometabolic effects in humans. Fifty physiologically controlled rats received saline or remifentanil infusion 20-160  $\mu\text{g}/\text{kg}/\text{min}$  for 3 hours followed 7 days later by neuropathologic evaluation. Four human volunteers underwent induction of anesthesia with propofol and rocuronium administration followed by remifentanil infusion at 1-3  $\mu\text{g}/\text{kg}/\text{min}$  with PET evaluation of Cerebral Metabolic Rate of Glucose (CMRG). In rats, dose related EEG activation was evident in all rats receiving remifentanil and 19 out of 40 remifentanil-treated rats showed brain damage, primarily in the limbic system ( $P < 0.01$ ). In humans, CMRG in the temporal lobe increased from  $6.29 \pm 0.32$  to  $7.68 \pm 1.05$   $\text{mg}/100\text{g}/\text{min}$  ( $p < 0.05$ ). These data indicate that prolonged high-dose remifentanil infusion is neurotoxic in rats with congruent metabolic effects with brief infusion in humans and suggest that some adverse effects reported in rats may be clinically relevant.