Involvement of 5HT2A receptors in the adverse interactions between opioids and serotonin-promoting drugs in rats

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In addition to addictive potential, opioids have neurotoxic risks in patients with mental problems concurrently using serotonin (5HT)-promoting drugs including SSRIs and MAOIs. The purpose of the present investigation was to test that 5HT2A receptors are responsible for such neurotoxic responses. Furthermore, we hypothesized that a major risk factor for neurotoxicity is the nature of external environment, in which warm temperature would enhance the responsivity of 5HT2A receptor responsible for inducing the toxicity. The hypothesis was thus examined at ambient temperature of 22 °C in contrast to 32 °C. The reference drugs used in this study included the opioid receptor agonist morphine, the serotonin reuptake inhibitor paroxetine and monoamine oxidase inhibitor clorgyline. Changes in brain 5HT were determined using microdialysis while brain activity was measured with electroencephalogram (EEG). Morphine alone injected into rats caused a small increase in 5HT in the cortex. However, the increase became excessive as injected concurrently with either paroxetine or clorgyline. Despite this, morphine in combination with paroxetine or clorgyline had little effect on brain activity measured with EEG recording at 22 °C. In contrast, seizure-like EEG activity was induced as the drug injections were made at 32 °C. To reveal the involvement of a specific receptor, effects of DOI (a 5HT2A receptor agonist) and 8-OH-DPAT (5HT1A agonist) were examined. Injection of DOI at 32 °C produced seizure-like EEG activity similar to opioid intoxication. The results of our data support the involvement of 5HT2A receptors in opioid-induced neurotoxicity in a temperature dependent manner.

Biography

Rui Tao earned his PhD in 2000 at Rutgers University of New Jersey and then joined the Department of Psychology at Harvard Medical School before he becomes a faculty member in the Department of Biomedical Science, Charles E. Schmidt College of Medicine, Florida Atlantic University. He has published 36 manuscripts regarding drugs of abuse including opioids, cigarette nicotine, cannabinoids and ecstasy MDMA.

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