

Researchers discover asphyxia trigger in opioid poisoning

January 26 2011, By Paul Cantin

Researchers at the University of Toronto have discovered a new way to combat asphyxiation caused by opioid poisoning, by “rescuing” a part of the brain which controls breathing. Having determined the mechanism of action of opiate suppression of breathing, the effectiveness of a commonly-used drug like naloxone provides a target for further drug development.

In a paper published in the *Journal of Neuroscience*, a team including researchers from the University of Toronto and the University of Alberta, say they have identified a potential means to combat the growing problem of opioid poisoning resulting in asphyxia.

Opiates are among the oldest known drugs in the world, with recognition of their beneficial effects (especially the analgesic - painkilling - properties) and therapeutic use predating recorded history. Throughout the centuries, however, the dark side to these drugs has also been well recognized: [opioid drugs](#) have addictive potential and they have toxic side effects.

According to the U.S. Centers for Disease Control and Prevention, opioid analgesics are involved in about 40 per cent of all poisoning deaths in North America. Deaths related to opioid drugs are increasing in Canada. In 2009, the Canadian Medical Association Journal reported that in Ontario, there has been a two-fold increase in opioid-related deaths over the last 16 years, since the introduction of long-acting oxycodone to the provincial drug formulary.

“Asphyxia caused by severe under-breathing and ‘respiratory arrest’ is the most serious side effect produced by opioids. For centuries however, the critical site in the brain where opioid drugs critically affect breathing was not known,” said Professor Richard Horner, of the Department of Medicine, Department of Physiology and the Canada Research Chair in Sleep and Respiratory Neurobiology.

In the article, Horner, along with Gaspard Montandon and their colleagues, determined that a small collection of cells within the medulla oblongata - the section of the brain which controls vital bodily functions - is critical for maintaining breathing, but also sensitive to opioids. This region, known as the pre-Botzinger Complex, can trigger asphyxia under the influence of opioids.

The cells in this region of the medulla oblongata that are affected by opioids have a chemical constitution that is distinct from other cells in this region. The goal is to specifically target these cells to reactivate them in the presence of opioids. Such a strategy would preserve the beneficial painkilling properties of these drugs but prevent the potentially lethal side effect of respiratory arrest.

“The good news is our research demonstrated that the respiratory distress can be rescued by the introduction of the drug naloxone, which reverses the effects of opioids,” Horner said. “These findings are essential to develop new pharmacological approaches to prevent life-threatening respiratory depression, without reducing the beneficial analgesic properties of opioid drugs.”

Provided by University of Toronto

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