



American College of Neuropsychopharmacology

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Safer opioid drugs could treat pain and save lives

Opioid drugs are the most widely prescribed and effective type of pain medication. But they are highly addictive and have some unpleasant and potentially deadly side effects.

Now a group of researchers, led by Dr. Laura Bohn at The Scripps Research Institute, may have found a way to make opioids safer by separating the drugs' pain relieving effects from their most dangerous side effect, respiratory suppression, which, in very severe cases, causes patients to stop breathing and to die.

All opioid drugs elicit their effects via a small group of protein receptors, called opioid receptors. When an opioid drug binds to its receptor, the receptor is activated and kicks off a chain of reactions that relieve pain. However, the activated opioid receptor can also interact with other nearby signaling proteins, causing side effects such as nausea, sedation, constipation or, most seriously, respiratory suppression.

Dr. Bohn's team has identified several molecules considered to be "biased agonists" because they act at the opioid receptor to stimulate pain relief, but cause less stimulation of the pathway that leads to respiratory suppression. In preliminary studies using mice, the researchers found that the most promising of these compounds provided pain relief levels similar to morphine, but with significantly less respiratory suppression.

Such opioids could help patients and doctors deal with drug tolerance, a frequent complication in which, over time, patients lose sensitivity to the pain-blocking properties of opioids and require higher doses to treat their pain. While biased agonists may be able to be used more safely at higher doses than other opioids, it remains to be seen how other side effect profiles will be affected.

One compound identified as a biased agonist—from the company Trevena—is already showing promising results as it makes its way through clinical trials, and the researchers hope that new compounds with stronger biases will yield even better results.

The recent epidemic of opioid-related deaths has been driven primarily by use of illegally made opioid drugs. However, prescription opioids are playing a significant role in the epidemic. As opioid overdose deaths are mostly due to respiratory suppression, safer

prescription opioids, such as those being developed by Dr. Bohn, could also ultimately decrease the number of deaths caused by abusing prescription opioids.

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