

Key discovery paves the way for new analgesics without adverse effects

Despite its strong efficacy against pain, morphine intake is associated with significant side effects such as constipation, nausea, vomiting, respiratory depression, addiction... The research team of Professor Alain Eschali r, Director of Neuro-Dol Inserm unit¹, member of the Analgesia Institute (Clermont-Ferrand, France), has just shown that it could be possible to dissociate these two effects, by maintaining the analgesic effect without any of the side effects.

The results of this study are published in Nature Communications, dated December 17, 2013.

Morphine is highly effective in treating some forms of acute and chronic pain. However its use is often limited by associated negative side effects. Both beneficial effects and side effects of morphine and other opioids are mediated by the same mu receptor. To date it has not been possible to dissociate them.

Neuro-Dol researchers hypothesized that working downstream of mu receptor on proteins called effectors, it could be possible to separate these two types of effects. They decided to focus on a potassium ion channel (TREK-1), an inhibitor of neuronal activity (which involvement in pain had previously been shown, together with M. Lazdunski and J. No l from IPMC in Sofia Antipolis, co-authors of the article), as a possible effector.

The purpose of their research was to show whether this channel could be involved in the analgesic effect of morphine without participating in its side effects. Their results show that:

- the analgesic effect of morphine is reduced in mice in which the gene has been deleted (KO TREK-1), including in models of clinical pain (eg postoperative pain); this reduction is even greater with fentanyl, another widely used opioid;
- the mu receptor has a functional relationship with the TREK-1 channel (electrophysiological study);
- constipation, respiratory depression, or physical dependence are not modified in KO TREK-1 animals.

These results confirm that TREK-1 channels are essential for the analgesic effect of morphine but are not involved in its adverse effects.

Direct activation of these channels could therefore lead to a morphine-like analgesia without inducing any of the side effects usually associated with this type of medication. This hope must be confirmed by further studies already initiated by the research team.

Besides new molecules specifically activating TREK-1 channels have been synthesized and are under evaluation within the Analgesia Institute, particularly in collaboration with the chemists of the CESMA team (Institute of Chemistry of Clermont-Ferrand), under the responsibility of Professor Sylvie Ducki².

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Sources

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- BioWorld <http://www.bioworld.com/content/trek-1-shows-potential-according-study>
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About the Analgesia Institute

In 2014, the Analgesia Partnership³ cluster becomes the **Analgesia Institute**, first initiative in France dedicated to research and innovation against pain. Located in the Auvergne, the Analgesia Institute stems from a commitment of excellence, with the establishment of a national network, and towards an international outreach.

The ambition of the members and partners of the Institute is to fight against pain, by developing innovative analgesics, safe, effective and more personalized.

The strategy of the Institute aims at valuing the plurality of the skills in order to emerge new concepts and to accelerate their transfer to therapeutic applications based on:

- efficient partnerships (preclinical/clinical, private/public ...)
- translational research, multidisciplinary and foremost patient-centred,
- efficient and shared platforms,
- teams working within a national network,
- an international Scientific Committee, ensuring excellence of the Institute 's research and innovation.

The Institute thus aims at promoting transdisciplinarity to feed the basic research and to develop clinically relevant concepts.

To this end, it will implement partnerships to unite widely around the fight against pain: research & care teams, learned societies, patient associations, industrials from pharma & nutrition (in human and animal health) and from any areas in a CSR approach, citizens...

Each entity wishing to invest in innovation against pain or wishing to be part of a meaningful societal approach, will reckon the Analgesia Institute as a perfect partner!

³The Analgesia Partnership cluster gathers 13 members:

Private structures

- AEPODIA
- ANS Biotech
- APTYS Pharmaceuticals
- CARBOGEN AMCIS
- CERB
- CREAPHARM
- NEURONAX
- NEUROSERVICE

Public structures

- UMR 6296 – team CESMA of ICCF (CNRS/ENSCCF/UBP)
- CIC 501 (CHU)
- CREPTA (CHU)
- ICOA (UdO)
- UMR 1107 – team PFCD of Neuro-Dol (Inserm /UdA)

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