MedicalXpress

Testing pain killers on humans could save money and speed the arrival of new drugs

November 8 2012

Deliberately inflicting carefully controlled painful stimuli on human volunteers and seeing how well specific drugs reduce the feeling of pain can be an effective way of testing new drugs. So conclude two researchers who reviewed the available literature on these types of tests in a paper published in the *British Journal of Pharmacology*.

Pain is important. It acts as an alarm mechanism, warning us that something is about to cause physical damage. It could be triggered by something physical like a cut or bruise, or a temperature driven stimulus such as extreme heat or cold. It could be caused internally by injuries where nerves get trapped. Pain can also become a long-term sensation that lasts long after the damage has occurred. In this case it is referred to as 'chronic' pain, and this can be particularly hard to treat.

The need to tackle pain is huge. A fifth of Europeans suffer from daily pain requiring treatment, with the proportion increasing in people over 70 years old. But pain control is still often insufficient or unsatisfactory because the available drugs fail to provide adequate relief or produce major side effects. Pain has therefore remained one of the major healthcare problems generating estimated socio-economic costs of $560-635 billion/year in the USA alone.

Finding new drugs is complicated because you can't measure pain directly. In animal models you have to watch animals as they respond to stimuli, and in human trials you have to get individuals to report how they feel. On top of this, the body has a number of different ways of

detecting pain- generating stimuli, and each mechanism is likely to respond to a different set of pain-killing drugs.

Based in Frankfurt am Main, Germany, Bruno Georg Oertel and Jörn Lötsch started out with a theory. "We thought that if a pain-relieving drug was effective in a particular experimental pain model and also in a specific type of clinical pain, then the experimental model should be predictive for the particular clinical setting," says Lötsch, who works in the Institute of Clinical Pharmacology at the Goethe-University.

They found that overall, human experimental pain models were able to predict how well a drug worked in patients better than previously realised. "Not using these pain models in drug development seems to be unjustified – in fact they should be used routinely in drug development programmes," says Oertel, who works in the Fraunhofer Project Group for Translational Medicine and Pharmacology (TMP), an initiative supported by the Hessian Excellence Initiative ("LOEWE") that runs at the junction between pharmacological research in academia and in the pharmaceutical industry.

The process isn't simple though as not every model can predict every clinical setting. "However, by analysing the way that drugs work in experimental and clinical settings, we identified that different sets of experimental pain models, rather than single models, may be best suited to provide cost-effective yet predictive studies in analgesic drug development," says Lötsch.

"It is difficult and unusual to undertake truly translational research in pharmacology. Here, Jörn Lötsch and Bruno G. Oertel have focused on experiments on humans to bridge the gap between animal research and clinical pharmacology. The review examines how well clinical analgesia is predicted by human experimental pain models, with a view to guiding model selection in phase I studies. The authors identify important

disparities between drug effects on experimental and clinical pain. This will help inform thinking on the refinement of human and animal models of pain, ultimately helping the pharmaceutical industry bridge the translational gap in the pain field," says Editor-in-Chief of the *British Journal of Pharmacology*, Professor Ian McGrath.

More work is needed before this approach is fully ready to use, but the researchers believe this could lead to a more cost effective approach that can help scientists gain valuable information about the ways new drugs are working.

More information: Bruno Georg Oertel and Jörn Lötsch; Clinical pharmacology of analgesics assessed with human experimental pain models: Bridging basic and clinical research; *British Journal of Pharmacology* 2012; DOI: 10.1111/bph.12023