

## Human pain experiments as an alternative to animal models

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A variety of **animal models** have been developed to explore the pain system and to investigate the efficacy of analgesics. However, preclinical pain models do not properly predict the clinical efficacy in humans and very few have been able to mimic the response to analgesics in man. This can be explained with species differences in receptor properties, pharmacokinetics and central pain mechanisms. Furthermore, animal studies are mainly based on motor reflexes or behavioural responses and such data can only partly be interpolated to human pain, which is a net result of complex sensory, affective, and cognitive processing.

On the other hand, **clinical pain** in patients is accompanied by several factors such as fear, emotions, anxiety, cognitive and autonomic responses, general malaise etc. influencing the overall sensory experience. Hence, when pain intensity is assessed with questionnaires it does not correlate well with the severity of the pathological condition. For example can improvement in e.g., depression during treatment result in less pain ratings.

**Experimental pain** in healthy volunteers or in well-defined patient groups makes it possible to overcome some of the abovementioned bias and therefore appear to be better suited to investigate the analgesic effects. The basic concept in these models is to control the stimulus and assessment parameters. It is essential that intensity, duration, frequency and localisation of the experimental stimuli be controlled. To mimic the clinical situation where many mechanisms come into play, different modalities (electrical, thermal, mechanical or chemical) are typically used in superficial and deep tissue. A combination of subjective measurements with objective assessments using e.g., cerebral evoked potentials, nociceptive reflexes or imaging to assess the multiple dimensions of pain is therefore a better solution. This mimic the clinical situations to a better extend, and in these models the effects of analgesics have been consistently reported.