Laser as a "Pain Inductor" to measure analgesic effects of pharmaceutical compounds

Pain measurement by sole subjective rating is invalid in patients. Such measures are not suitable for detailed investigation of peripheral and central pain processing and the same holds for the efficacy evaluation of analgesics. But the human black-box should allow additional drug investigations of objectives as general efficacy principles or dose-time efficacy.

A major enhancement to measure pain processing and analgesia under the prerequisites "Induce pain to measure pain" was established in the last two decades by introduction of Laser technology. Pain measurements need short-term temperature raises at skin level (>43°C Celsius) to overcome the thresholds of heat-sensitive nociceptors to get painful sensation. Such stimulations are only manageable in experimental conditions by Laser devices, used on normal or sensitized skin, introducing local UV or capsaicin exposure to generate somatosensory evoked potentials (SEP) from Vertex-EEG by triggering, filtering and averaging of artifact-free painful stimuli. Long-lasting impacts as slow acting cold-warm and chemical stimulations, but also short-lasting impulses, e.g. electric ones, are no suitable pain triggers and are not devoid of inherent unspecific influences – leading to negative outcomes.

Laser-SEPs can be used for following interpretations:

- Determination of sensory stimulus-intensity relationship (efficacy)
- Localizing type and pathways of pain-processing (peripheral and/or central preference)
- Quantification and comparison of different analgesics and combinations (dose-time efficacy)

A similar approach and differentiation can be introduced by the additional use of different skin conditions (normal, UV and capsaicin skin). Further the main components of the Laser signal (N2- and P2-amplitude, see Fig.1) can be attributed to predominant peripheral and/or central-spinal pain processing.

Examples for compound classes investigated with the (objective) Laser model up to now are the following:
- NSAIDs, opioids, cannabinoids, antihistamines, antidepressants, antiepileptics and diverse blockers, topicals.
- The attenuation of Laser-induced pain on UV skin by the antiepileptic Pregabalin (red) vs. placebo (blue) is demonstrated as an example in Fig. 2.
- The Laser allows answering of questions on compound efficacy in different types of analgesics with small groups of healthy subjects (e.g. 18 - 24 people) in an ethically acceptable approach without additional impacts on suffering patients in clinical pain situations. Laser studies are time- and cost-saving, can be part of proof of concepts (PoC) in drug development and of Go/No-Go decisions, thus distinctly reducing expenses of subsequent extensive patient studies.

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