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Future of Neuroimaging as Pain Scanners in Marker Development of Pain

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Abstract

In clinical practice, pain is asked by the physician to be narrated with some specificity but is found that quite often the patient's narration of pain is very vague. There is no pain thermometer to gauge the intensity of pain. This makes it interesting to research if imaging can help in seeking quantifiable pain markers. The preclinical and clinical trials on pain have both ethical and medical considerations and are not easy to quantify. Imaging modalities like fMRI or PET, along with machine learning techniques, may play an important role in defining the changes in the brain according to the intensity of pain. It is also of significance to find if there are changes in pain perception in an individual as per neuroleptic modulation with the ageing brain. The markers for pain should be reproducible and measurable and consistent to subjective self-report of the patient.

Keywords: Markers; Neuroimaging; Pain

Abbreviations: fMRI: Functional MRI; PET: Positron Emission Tomography; CNS: Central Nervous System

Introduction

Pain has been associated with humans in one form or the other, whether it is structural or visceral. The importance of markers in early intervention of diagnosis and response to therapy is well documented [1]. Pain Markers have been evaluated to be quantified and some approach to quantify them have been made [2]. Research is usually done on the hypothesis that markers can be quantified and if we could define the pain markers. The present standards to measure pain clinically are self-reported by the patient, that could be deemed as unreliable and the need to quantify these with suitable markers has always been there. There are certain imaging modalities that could help in defining such markers and to eventually quantify them.

CNS Imaging Modalities for Pain Assessment

fMRI is now used, more than before, to understand the quantitative biomarker mechanism for a drug development and even provide in-depth insight to pharmacokinetics and pharmacodynamics. fMRI is a good approach to the proof of concept but is an expensive imaging modality. BOLD (Blood Oxygen level dependent signal) is one of the very commonly used fMRI technique to identify activity in different areas of the brain on a stimulus [3].

PET is another technique to functionally characterize the changes in brain with pain perception and is also a tool to look for quantifiable bio-assay.

Both fMRI and PET are non-invasive radiological and molecular imaging techniques, objective to measure but

still we do not have sensitive and specific pain markers [4].

Rationale of Neuroimaging in Pain

Neuroimaging can possibly replace the variable subjective self-reporting of pain by the patient by providing an objective assessment of the intensity of pain. This will not just be important from a diagnostic point of view, but will be of immense help in managing the pain. These pain markers will provide a quantitative assessment and qualitatively change the management of such patients. The pain markers that the researchers are seeking must have good diagnostic values, should be quantifiable (test-retest reliability) [5], and are validated through further examinations. This requires rigorous research efforts. An approach to decode the neuroimages and look for an acute or chronic pain would help further in getting closer to the relevance of neuroimaging in pain.

Inflammatory and Neuropathic Pain

The two types of pain in inflammation and neuropathic conditions are not the same and has been differentiated well by a study done by Gineste et al. and exhibiting the role of the drug, nimesulide, as an anti-nociceptive agent [6]. Cystatin C levels in cerebrospinal fluid could possibly indicate a varicellazoster virus post herpetic neuralgia [7,8]. The duration and intensity of pain and its correlation with Cystatin C are not suggestive of any correlation between the two [8]. Pain markers for chest pain, obstetric pain, or relevance of pain with irritable bowel syndrome (IBS) will be different from neuropathic or inflammatory pain. Labus et al. collaborated on the neuroimaging biomarker with IBS [9]. This opens a vast potential for a difficult research paradigm to study different pain markers.

Conclusion

A great deal of study is required into a search for effective, reproducible and measurable pain markers. Some believe that pain markers do not have reliability but others think that pain perception may be affected by our prior experiences, our reaction to pain stimulus and our storage of this stimulus within our brain. Whatever we feel about pain should be quantifiable on imaging and if this is achieved, then we can certainly make changes to the diagnostic and prognostic values in our patients. Time and more research can only tell if fMRI and PET or some other new discovered imaging tool becomes the modern pain scanner and if the pain would transition from a symptom to a self-contained disease diagnosed through these pain scanners.

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