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Editorial comment

A possible biomarker of low back pain: ^{18}F-FDeoxyGlucose uptake in PETscan and CT of the spinal cord

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In this issue of the *Scandinavian Journal of Pain*, Zhou and co-workers publish an interesting study demonstrating that patients with low back pain (LBP) appear to have increased metabolic activity in the lower thoracic and upper lumbar segments of their spinal cord, compared with patients of same age and sex who do not have LBP [1].

The findings by Zhou et al. implicate that patients with LBP can be differentiated from people without LBP, using PET/CT scan. The uptake of 18F-FDG as PET ligand has a potential as a biological marker of increased metabolic rate in that area.

The increased metabolic rate detected in the affected areas of the spinal cord may represent a process of excitation in the dorsal horn neurons, and/or a visualisation of a neuro-inflammatory process affecting this part of the spinal cord. Both these processes have been claimed to be important for the development of chronic pain. These claims are likely to be true, but there have been very little direct evidence that these phenomena actually take place in patients. The observations made by Zhou et al. are interesting in this respect.

The results represent an objective diagnostic finding in the clinical evaluation of patients suffering from LBP. The findings may have a potential for guidance to better diagnosis, and help for development of better treatments, in order to improve the situation for chronic pain patients.

1. Importance of objective biomarkers for chronic pain

Years lived with disability (YLDs) is a measure of non-fatal health outcome, and pain conditions caused 21% of all YLDs globally [2]. Low back pain, the pain diagnosis explored in this study by Zhou et al., was the leading single cause for YLD followed by depression, anaemia, and neck pain. Thus, low back pain obviously represents a wide spread disease in the world's population.

Some years ago, in an assessment of different treatments against low back pain, that were offered by "school medicine" and private health care providers, 48 different treatments were listed as being in current use, varying from multimodal pain rehabilitation, analgesic medication, fusion surgery, trigger point blocks, to psychotherapy, hot baths or herbal medicine. All of them were claimed to give relief by the caregivers using the methods, even if the scientific support usually were slight or absent [3]. Even if the knowledge have increase a bit during the last 15 years, this obviously indicates that we have a lack of understanding about the underlying processes actually causing the pain in the low back.

Almost all medical specialties have a foundation in analysis of biomarkers for diagnosis of diseases, and as a guide for treatment choice and treatment effects. In contrast, in the field of pain medicine, there are up to now few or no biomarkers to rely upon. In the pain field, the golden standard of pain assessment is based upon the patients self-report and clinical investigations, but objective, measurable findings are usually absent.

Of course we must trust the patients report, but I often wish that we had better tools to understand the nature of pain related processes, and their pathophysiology. Perhaps biomarker studies in body fluids, e.g. in blood [4], CSF, saliva, or micro-dialysate from painful tissue, or, as in this study by Zhou et al., image biomarkers [5,6] can help us to a better understanding of what actually is going on in the pain patients from a pathophysiological point of view? Could some aspects of these complex processes involved be objectively measured using biomarkers?

2. What is a biomarker?

One frequently used definition says: ". . . a biomarker is a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention" [7]. So far, we have no established validated biomarker to use in pain patients, but the candidate biomarkers presented so far, give some hope for the future.

3. Strong sides of this study

I think that Zhou et al. has used a very clever approach in this study. They have "re-used" data from more than three thousand

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18F-FDG PET/CT scans, done in patients because of cancer diagnostics, and from them, by retrospective use of health questionnaires, identified a group of 13 patients suffering from low back pain, and 13 as matched pain free controls. This is a good way to extract information from data that is "already there", to produce fruitful results stimulating to deeper studies. There is also an economical aspect-the 26 PET/CT scans carried out here would cost around 26 000 US $. In this study this cost was already paid.

4. Limitations of this study

This retrospective, "re-use-design" also introduces some limitations of the present study. The pain problem that these patents suffered from is not described well, but only as: "do you have low back pain – yes or no". This is certainly not detailed enough, but may anyway provide some useful information. The study was originally not designed as a study of low back pain. The number of subjects included in the study is small, and of course it needs to be repeated in a larger cohort with a better design.

5. Conclusions and implications

Nevertheless, the study Zhou et al., indicate that research on spinal cord image biomarker in pain patients, using PET/CT methodology, may contribute to a better understanding of the biological aspects of the complex pathophysiology of pain. Their investigation demonstrates that pain related processes in the spinal cord may be objectively visualized and quantified with PET/CT imaging. It represents a good early attempt in the search for Identification of an image biomarker in defined clinical pain conditions. The findings may have substantial potential on guidance for better diagnosis, and help for development of better treatments in order to improve the situation for chronic pain patients.

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