Scandinavian Journal of Pain 4 (2013) 171–172

Contents lists available at ScienceDirect

Scandinavian Journal of Pain

journal homepage: www.ScandinavianJournalPain.com

Editorial comment

Chronic pain – The invisible disease? Not anymore!

Torsten Gordh*

Multidisciplinary Pain Center, Uppsala University Hospital, Uppsala, Sweden

In this issue of the *Scandinavian Journal of Pain*, in the article "**New objective findings after whiplash injuries: High blood flow in painful cervical soft tissue: An ultrasound pilot study**" Hatem Kalawy and co-workers [1] describe an objective finding in localized sites where the patients experience pain. In patients suffering from chronic neck-pain following whiplash associated disorder (WAD), all regions identified by the patients as painful and tender corresponded to areas showing increased high blood flow, documented by gray scale ultrasound and colour Doppler examinations. The findings raise the possibility that chronic neck pain in WAD is related to the areas with high blood flow.

1. Objective findings in whiplash-associated pain

This observation of increased blood-flow in painful neck-areas may become very important, both for the diagnostics of pain patients, for a better understanding of the pathophysiology of chronic pain, and especially for these unfortunate WAD-patients who too often are met with disbelief by health care providers and insurance people.

2. We do not know why acute pain becomes chronic pain

The exact pathogenesis of most kinds of chronic pain is largely unknown. For instance, what are the actual contributions and importance of peripheral and central mechanisms to the total experience of pain? How important is the nociceptive input from peripheral tissue, where the pain is localized by the patient, and what is the contribution of the excitatory processes in the central nervous system, leading to an increased response in the spinal and cerebral "pain matrix" to peripheral pain impulses? We, in fact, do not know this when facing individual patients.

3. "Central hypersensitivity" – a pseudo-explanation?

There are few diagnostic tools for chronic musculoskeletal pain; structural imaging methods seldom reveal pathological alterations. Radiologic modalities such as a radiogram, CT, and MRI usually cannot identify any pathology [2]. We tend to explain the pain as caused by processes in the central nervous system; we tell the patients and ourselves "... the cause of the pain has become centralized" [3]. This, however, does not exclude the existence of peripheral tissues pathology that is causing pain and is not detected by these diagnostic modalities. Most probably, the chronic pain is due to both these processes working together – a peripheral nociceptive input is "driving" central sensitization processes of different kinds that in turn amplify the nociceptive message from the periphery.

4. fMRI and PET scan are increasing our understanding of pain modulation

At present, we know more about the central processes that may be detected by neurophysiological methods [4] and by brain imaging studies [5]. Many brain activation studies using fMRI and PET have now shown distinct patterns of "abnormal" brain activation in patients with chronic pain syndromes [6], including WAD patients [7,8].

5. Without "objective signs", we do not always believe chronic pain patients

Pain is a uniquely personal experience, and self-reports from the patients remain the gold standard of assessment. However, patients and doctors often are somewhat uncomfortable with this situation, and would be happy if there were some "objective signs", corresponding to the site(s) of experienced painful sensation. The clinical scenario often looks something like this:

> The WAD patients may be told, "There is nothing wrong, the X-ray examinations are all normal". This may be difficult to accept for the patient, since there is an obvious pain sensation in the back of the neck. We, pain doctors, usually try to explain to the patient that the lesion in the neck after the whiplash accident now has healed, because wounded tissue usually do so after some months, and definitively after some years, to the best of our knowledge. Instead, we tell the patients that their chronic pain is mainly due to changes that occurred in the central nervous system, e.g. central sensitization and disinhibition that followed the initial trauma some years ago. These CNS-processes amplify normal sensations of small painful stimuli to

DOI of refers to article: http://dx.doi.org/10.1016/j.sjpain.2013.06.006.
* Corresponding author. Tel.: +46 706244894.
E-mail addresses: torsten.gordh@surgsci.uu.se, torsten.gordh@akademiska.se

http://dx.doi.org/10.1016/j.sjpain.2013.07.024

become subjective experiences of strong pain in the neck. "But, there is actually nothing wrong in the neck itself".

Well, this is probably all true, at least partly, but we actually do not know for sure that there is "nothing abnormal going on" in the peripheral tissues. No one has really provided positive evidence for that [1,9].

6. Recent objective findings of pathology in the neck of WAD-patients

Recent studies actually indicate ongoing pathological processes in the peripheral painful areas in the neck in WAD-patients.

1. Whiplash patients have signs of local persistent peripheral *tissue inflammation* in the painful areas [9]. That investigation demonstrated that pain-associated processes in peripheral tissues can be objectively visualized, objectively quantified, and objectively followed over time with PET-CT [9]. [11C]-D-deprenyl seems to be a promising tracer for these purposes. Thus, D-deprenyl accumulates in inflamed joints in patients with rheumatoid arthritis [10].
2. An MRI study documented that fat infiltrates the cervical extensor muscles in patients with persistent whiplash-associated disorders [11]. This is not found in patients with spontaneous neck pain with no trauma [12].
3. The **new findings** of high blood flow in painful cervical tissue by Kalawy et al. [1] presented in this issue of *Scandinavian Journal of Pain* thus add new information to the concept that "something is going on" in the peripheral tissue where the pain is experienced, findings that are not found in pain free control persons.

7. Neovessels in painful neck-areas in patients with whiplash-associated disorder (WAD)

The idea to investigate WAD patients with the ultrasound/Doppler method arouse from earlier observations by Alfredson's group [13]. They documented vascular proliferative changes in chronic painful tendinosis [13]. They now documented similar changes in the chronically painful neck areas of 20 patients with WAD [1]. All patients had normal plain radiograms of the neck, and in the 12 patients in whom MRIs were obtained, the MRIs of their necks were normal.

In spite of normal neck-X-rays and MRIs, *gray scale ultrasound and colour Doppler* documented significantly more regions with high blood flow in the WAD-patients compared with 20 control subjects without pain [1]. At all levels of the neck, the high blood flow patterns were detected at the *muscle-tendon entheses at the spinous processes*, and bilaterally they were *juxtapositioned to the facet joints*. All regions identified by the patients as painful and tender corresponded to the areas of high blood flow found during the ultrasound/Doppler examinations. The findings raise the possibility that chronic neck pain in WAD-patients in some way is related to the regions with high blood flow. The study was single-blinded; therefore, a future double-blinded investigation should verify these interesting and important results.

In spite of this weakness of the study, together with other objective findings with different techniques [9,11], the new findings presented by Kalawy et al. [1] strengthen the idea that changes in peripheral tissue contribute to chronic pain in WAD patients. The vascular changes were found in the chronic phase, more than two years after the initial injury, a similar finding as in the PET study [9] indicating some degree of ongoing inflammation and/or degenerative processes similar to those found in chronic tendinosis. The exact nature of the changes is not yet known, but a persistent inflammation in combination with vascular proliferation and fatty infiltration are objective features.

8. Conclusion and implications

Objective visualization of local processes following peripheral tissue injury, probably involved in the generation of nociceptive input, may strengthen patients' self-report and add to the methods used for diagnostic work-up for chronic pain patients. It may also stimulate to a shift of focus in pain research, to the importance of peripheral nociceptive input as a generator of chronic pain, most likely acting in concert with central sensitization processes [14]. The new findings by Kalawy and co-workers [1] are important contributions to this field of research.

References

[1] Kalawy H, Stålnacke BM, Fahlström M, Öhberg L, Linetsky F, Alfredson H. New objective findings after whiplash injuries. High blood flow in painful cervical soft tissue: an ultrasound pilot study. Scand J Pain 2013;4:173–9.
[2] Borchgrevink GE, Smevik O, Nordby A, Rinck PA, Stiles TC, Lereim I. MR imaging and radiography of patients with cervical hyperextension-flexion injuries after car accidents. Acta Radiol 1995;36:425–8.
[3] Phillips K, Clauw DJ. Central pain mechanisms in chronic pain states—maybe it is all in their head. Best Pract Res Clin Rheumatol 2011;25:141–54.
[4] Curatolo M, Petersen-Felix S, Arendt-Nielsen L, Giani C, Zbinden AM, Radanov BP. Central hypersensitivity in chronic pain after whiplash injury. Clin J Pain 2001;17:306–15.
[5] Tracey I, Mantyh P. The cerebral signature for pain perception and its modulation. Neuron 2007;55:377–91.
[6] Apkarian AV, Bushnell MC, Treede RD, Zubieta JK. Human brain mechanisms of pain perception and regulation in health and disease. Eur J Pain 2005;9:463–84.
[7] Linnman C, Appel L, Furmark T, Söderlund A, Gordh T, Långström B, Fredrikson M. Ventromedial prefrontal neurokinin 1 receptor availability is reduced in chronic pain. Pain 2010;149:64–70.
[8] Linnman C, Appel L, Söderlund A, Frans O, Engler H, Furmark T, Gordh T, Långström B, Fredrikson M. Chronic whiplash symptoms are related to altered regional cerebral blood flow in the resting state. Eur J Pain 2009;13:65–70.
[9] Linnman C, Appel L, Fredrikson M, Gordh T, Söderlund A, Långström B, Engler H. Elevated [11C]-D-deprenyl uptake in chronic Whiplash Associated Disorder suggests persistent musculoskeletal inflammation. PLoS ONE 2011;6:e19182.
[10] Danfors T, Bergström M, Feltelius N, Ahlström H, Westerberg G, Långström B. Positron emission tomography with 11C-D-deprenyl in patients with rheumatoid arthritis. Evaluation of knee joint inflammation before and after intra-articular glucocorticoid treatment. Scand J Rheumatol 1997;26:43–8.
[11] Elliott J, Jull G, Noteboom JT, Darnell R, Galloway G, Gibbon WW. Fatty infiltration in the cervical extensor muscles in persistent whiplash-associated disorders: a magnetic resonance imaging analysis. Spine 2006;31:E847–55.
[12] Elliott J, Sterling M, Noteboom JT, Darnell R, Galloway G, Jull G. Fatty infiltrate in the cervical extensor muscles is not a feature of chronic, insidious-onset neck pain. Clin Radiol 2008;63:681–7.
[13] Öhberg L, Alfredson H. Ultrasound guided sclerosis of neovessels in painful chronic Achilles tendinosis: pilot study of a new treatment. Br J Sports Med 2002;36:173–5.
[14] Staud R. Peripheral pain mechanisms in chronic widespread pain. Best Pract Res Clin Rheumatol 2011;25:155–64.