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Editorial Comment

The triumvirate of co-morbid chronic pain, depression, and cognitive impairment: Attacking this "chicken-and-egg" in novel ways

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In this issue of the *Scandinavian Journal of Pain*, Daniella Cha et al. have looked at the overlapping problems of depression, chronic pain and cognitive impairment in a unique way [1]. As they state, these three entities are well-known to be comorbid. As they also state, there has been an interest in looking at the three problems as a single entity, thus defining a specific phenotype that should be thought of as a single problem and that therapy for this phenotype could be more effective than therapies for the separate components. Since it is well known that treating only depression with comorbid pain is extremely difficult and treating only chronic pain with comorbid depression is extremely difficult, there is some sense in the proposition that a treatment for this "triumvirate" as they term it, might be more effective.

1. Interactions of pain (VAS), depression (MADRAS), and perceived cognitive deficit tested with THINC-it

Cha et al. have chosen to look at the interrelationship of depression, chronic pain and cognitive deficits in a unique way. Part of the uniqueness is having a cohort of depressed subjects and also a cohort of "normal" subjects. The group recruited from a general population was as a normative standard to be compared to the depressed group. It appears that some of the motivation for the study was also the need to further test their package, THINC-it, for the evaluation of cognitive deficits but it is fortunate that they have chosen this paradigm. The THINC-it package is a composite of several validated tests for cognitive function that this group has previously validated as a package in a study that has been submitted elsewhere.

By dissecting the possible interactions of depression (MADRAS), pain (VAS), perceived cognitive deficit and tested cognitive deficit (THINC-it), Cha et al. have come up with some very interesting conclusions, some obvious, some not so obvious [1].

(1) Pain discriminates between the depressed group and the non-depressed group,
(2) Depression severity predicts VAS scores,
(3) VAS level predicts the perceived cognitive deficit,
(4) VAS level predicts depression severity,
(5) This effect is cancelled out if one corrects for depression,
(6) Depression severity predicts perceived cognitive deficit,
(7) Perceived cognitive deficit predicts measured cognitive deficit,
(8) The combination of VAS plus perceived cognitive deficit is an even stronger prediction of measured cognitive deficit.

2. Perceived cognitive deficit is a hallmark of fibromyalgia ("Fibrofog"), but is present also in other chronic pain conditions

Much of this, i.e. the depression/pain interdependence, is not new [2]. However, the information concerning cognitive deficits is quite valuable in another way for those working with patients with both depression and pain. For many years, clinicians treating chronic pain were skeptical that patients with, for example fibromyalgia, actually had the cognitive deficits that they complained about until more sensitive testing was done. Now perceived cognitive deficits are felt to be a hallmark of fibromyalgia and are included in newer diagnostic protocols. Perceived cognitive deficits seem to be worse with higher pain levels in fibromyalgia as well as in this study's depressed cohort. Here we have some very strong evidence to support the experience of not only fibromyalgia patients but also many others with chronic pain as well as depression. "I can't think clearly", "I have trouble concentrating", "My memory is so bad" are very common comments from many pain patients with a variety of diagnoses. "Fibrofog", as it is called in the fibromyalgia literature, is not restricted only to those with fibromyalgia [3].

3. Neuroanatomical overlap of pain, depression, and cognitive deficits

Cha et al. discuss the theory that the "triumvirate" of depression, pain and cognitive deficits is due to structural changes in the brain and that those changes overlap areas common to all three

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problems. There is some evidence for this neuroanatomically with newer scanning techniques as Cha et al. point out [1]. They also wonder about possible effects of "inflammation" (chronic neuroinflammation?) and the "opioidergic" systems on neuroanatomy. But structure and function are separate and one can also look at the depression/pain/cognitive deficit problem from a more dynamic functional point of view. With regard to function, there is an alternative explanation that could stand alone or be complimentary to the structural change theory. In this issue of the Scandinavian *Journal of Pain* and in a 2013 article in the *Journal of Pain*, Kolesar et al. have elegantly outlined the function of the *Default Mode Network* in pain [4,5]. Altered function of this network which has connectivity to the neuroanatomical structures cited by Cha et al. could also explain the depression, pain, cognitive deficit codependence [1]. It is very likely that both structure and function are involved and these two cannot be separated [6,7].

Cha et al. point out that medications for both pain and depression can cause cognitive deficits as a side effect. Although the article does not include a list of medications and dosages, the authors remark that the subjects in the depression group were remarkably free from or had only low doses of medications and feel that this could not explain the cognitive deficits [1].

4. Successful treatment of both pain and depression should improve cognitive dysfunction

I agree with their **conclusion**, where Cha et al. emphasize that for patients with depression, simultaneous treatment of pain is needed because of their findings of comorbidity in their subject group of depressed patients [1]. They also suggest that treating both problems would improve the cognitive dysfunction that accompanies both states. Studies from the *Default Mode Network* literature actually support this. Several studies demonstrate that successful treatment for pain (medications, cognitive behavioural therapy, and spinal cord stimulation) actually resets the *Default Pain Network* back to normal functioning and it would be interesting to look at the same information from successful treatment for depression. Evaluation of cognitive function with THINC-it and the connectivity of the *Default Mode Network* with fMRI in future studies should give us some interesting new information.

Conflict of interest

None declared.

References

[1] Cha DS, Carmona NE, Mansur RB, Lee Y, Park HJ, Rodrigues NB, Subramaniapillai M, Rosenblat JD, Pan Z, Lee JH, Lee JG, Almatham F, Alageel A, Shekotikhina M, Zhou AJ, Rong C, Harrison J, McIntyre RS. Pain and major depressive disorder: associations with cognitive impairment as measured by the THINC-integrated tool (THINC-it). Scand J Pain 2017;15:62–7.
[2] Goesling J, Clauw DJ, Hassett AL. Pain and depression: an integrative review of neurobiological and psychological factors. Curr Psychiatry Rep 2013;15:421.
[3] Kravitz HM, Katz RS. Fibrofog and fibromyalgia: a narrative review and implications for clinical practice. Rheumatol Int 2015;35:1115–25.
[4] Kornelsen J, Sboto-Frankenstein U, McIver T, Gervai P, Wacnik P, Berrington N, Tomanek B. Default mode network functional connectivity altered in failed back surgery syndrome. J Pain 2013;14:483–9.
[5] Kolesar TA, Bilevicius E, Kornelsen J. Salience, central executive and sensorimotor functional connectivity alterations in failed back surgery syndrome. Scand J Pain 2017;15:10–4.
[6] Brodal AP. A neurobiologist's attempt to understand persistent pain. Scand J Pain 2017;15:140–7.
[7] Butler S. Important new insight in pain and pain-treatment induced changes in functional connectivity between the Pain Matrix and the Salience-, Central Executive-, and Sensorimotor-networks. Scand J Pain 2017;16:64–5.