[Guest Editorial]

for the November 2021 - Volume (59) of Sleep Medicine Reviews. Attached please find a pdf-file of the target article: “Cognitive Behavioral Therapy for Insomnia in Patients with Chronic Pain - A Systematic Review and Meta-Analysis of Randomized Controlled Trials” Selvanathan et al. - SMRV-D-20-00140.

Is cognitive-behaviour therapy for insomnia (CBT-I) the new best pain killer?

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Cognitive behavioural therapy for insomnia (CBT-I) is now firmly recognised as an effective treatment for insomnia, with experts and learned societies across several continents recommending it as first line treatment (1-5). The research horizon of the past couple decades has been expanded to apply CBT-I to physical and mental health conditions in which insomnia is a prominent presenting feature. The expectation is high: Apart from improvement in sleep, the secret hope we harbour is that CBT-I would be an agent of change that successfully tackles the comorbid condition that might have triggered, maintained, aggravated or be aggravated by insomnia.

One of these comorbid conditions is chronic pain, which is defined as pain that persists beyond the normal tissue healing time (6). Living with chronic pain is no easy business. Though invisible, the impact of pain impinges on normal life from working outside home, doing household chores, driving, walking to sleeping (7, 8). The majority of patients presenting at pain clinics have moderate to severe insomnia and see better sleep as a treatment priority (9, 10). With a new understanding that insomnia is not a mere symptom of chronic pain but a driver of this bidirectional relationship, CBT-I offers fresh excitement for the fight against chronic pain, for which even potent pain killers such as opioids are not a solution but the core of a new layer of problem (11, 12). Chronic pain management is at a crossroads. Recent reviews and syntheses of evidence have shown that interdisciplinary pain management programmes – a staple intervention offered in many health care systems – do not provide sufficient benefits on pain and other quality of life outcomes compared with usual care (13). Similarly, psychological treatments based on cognitive-behavioural principles only result in weak improvements in pain and depression at post-treatment, which attenuated even further at follow-ups (14). The field is keeping a hawk eye on whether CBT-I is the new best pain killer.

In this issue, Selvanathan et al. (15) provided empirical evidence right on this topic. The paper offered a timely update to a previous review on nonpharmacological treatments of insomnia for long-term pain conditions (16), to include several recently published trials (17-22) and to specifically appraise the utility of CBT-I for individuals with chronic non-cancer pain. The systematic review followed the gold standard methodology with a high level of rigour in the meta-analysis evaluating the effect of CBT-I on sleep, pain, depression, anxiety and fatigue.

The authors identified a total of 14 randomised controlled trials - involving 783 participants - eligible for the systematic review. Whilst all studies contributed to the meta-analysis of pain outcomes at post treatment, a smaller subset of studies were included for the analysis of sleep outcomes (n= 10 studies, 644 participants), depression (n= 8 studies, 383 participants), anxiety (n= 4 studies, 234 participants) and fatigue (n= 4 studies, 168 participants), and with an even more restricted pool of studies for the follow-up and sub-group analyses. There is a noticeable reduction in the size of the body of available data, as the outcome measures go beyond the diagnostic boundary and as the repeated assessments stretch over time. However, based on both quantitative and qualitative evaluations, the included trials were judged to be predominantly of high quality (11/14 studies considered as "excellent" psychological trials for chronic pain)(23). So, it is fair to say that this systematic review is no "garbage in-garbage out" (24, 25). It is instead the fruit of hard work of colleagues in the field.

On this basis, the authors found that CBT-I has a large treatment effect over controls on global measures of sleep (Standardised Mean Difference = 0.89 at post-treatment, 0.56 at follow-up) and specific sleep parameters measured with sleep diaries (SMD at post-treatment and follow-up for sleep onset latency = 1.06, 1.08; wake after sleep onset = 1.00, 0.87; sleep efficiency = 1.25, 1.1). Both the magnitude and statistical significance of these effects were sustained at follow-up (up to nine months), although as expected CBT-I - which often includes a sleep restriction component - had no significant effect on total sleep time. These findings chime well with previous meta-analyses (26-
28) showing that CBT-I can treat insomnia with success in comorbid physical and mental health conditions. Of greater importance is the finding that the effect of CBT-I went beyond sleep and generalised to pain intensity (SMD = 0.19), pain interference (SMD = 0.75) and depressed mood (SMD = 0.44) at post-treatment, even though these effects were reduced at follow-up. It is also worth noting that these treatment effects were at least on par with those reported by patients who completed CBT programmes specifically designed for pain management (SMD for pain: 0.09 vs active control, 0.22 vs treatment as usual; depressed mood: 0.09 vs active control, 0.34 vs treatment as usual) (14).

These findings are not strictly unexpected for those who have been following the literature, but it will be an empowering message to people: that their sleep can get better despite the continual presence of chronic pain. A caveat is that the improvement here only referred to people’s self-reported sleep experience, because for concerns of heterogeneity in technology and methodological procedure, the authors included self-reported patient outcomes only and there were no data on changes in sleep architecture and staging following CBT-I. The effects of CBT-I on polysomnographic measurements of sleep and neurological responding to threat remain to be determined in the future, whilst more trials incorporate physiological assessments as outcome measures (17, 19, 29).

It is puzzling - if not disappointing – that CBT-I’s effect on anxiety was not significant in chronic pain patients whilst it was for anxious patients (30) and that it was not effective in lifting fatigue as seen in trials of patients with cancer pain (16). The positive effect of CBT-I on pain was unfaible but appeared to be moderate and transient. CBT-I may take the edge off the pain for a while, but it remains an open question whether it offers the ‘system reset’ required to make inroads into the underlying pathological pain processes. Perhaps, these effects would be become more observable or stable once the pool of evidence has grown in size; the total number of participants pooled in the pain analysis was less than 1000. Perhaps, the reversal of the underlying pain processes takes more time and additional coordinating actions at different levels, in order to translate the benefits of improved sleep into reductions of inflammation, HPA axis arousal, and pain sensitivity; and to such an extent that the totality of these would be experienced as less pain and fatigue and better mood and functioning. To answer these questions, we will need trials with longer term follow-ups and the right design for evaluating bio-psycho-social mechanisms of change.

Perhaps, CBT-I is not the panacea of all ills after all, especially for complex comorbidities. If that is the case, it would be sensible to temper our expectations but continue to explore ways to enhance treatment effects and efficiency. This could be done with CBT-I as a starting point or as a supplement to existing treatment. A handful of trials (18, 19, 22) and pilot studies (31, 32) have taken the hybrid CBT approach to recalibrate the treatment with select sleep and pain management components. The idea is to achieve better results and higher efficiency by targeting both conditions and their interacting elements simultaneously (33). However, as is evident from the Selvanathan et al. (15) systematic review, such a development is still in its infancy and the existing studies are very different in their target pain populations, treatment content, dosage, length, format, delivery and setting. More research is needed to determine what an effective hybrid CBT for pain and insomnia should look like, when and to whom this treatment should be offered, what dosage and mode of delivery are most suitable, and what infrastructure is required for the cost-effective delivery of such intervention.

On the last point, both the global and local health and care landscapes are rapidly changing. Some of the technological advances have been unexpectedly accelerated by the COVID pandemic, which has turned telemedicine into a mainstream reality almost overnight even for the most resistant and reluctant corners of the health care system (34). It remains to be revealed in the post-COVID world how the treatment of insomnia and chronic pain stacks up against the treatment of other health
conditions in terms of priorities and its share of available resources, but it seems a safe bet that the future of chronic condition management will involve a greater degree of telemedicine and online delivery (35), for not only scaling and cost considerations but also for reasons of infection control. All of the trials included in the Selvanathan et al. (15) systematic review were delivered face-to-face, be it individually or in groups. Significant investment in remote CBT-I tailored to the specific needs of various chronic pain populations will be a necessary manoeuvre to catch-up with the changing landscape, although the medium of delivery (phone calls with trained therapists, video chats, interactive online platforms), degree of AI algorithms (vs human touch) and standardisation (vs flexibility) are still matters of personal taste and opportunities for innovation.

Overall, the evidence presented in Selvanathan et al. (15) has given confidence to the view that, for people with chronic pain, sleep is a viable alternative treatment entry point. The paper offers a neat illustration of the reciprocal pain-sleep relationship in the positive domain, whereby we can expect an improvement in pain following an improvement in sleep (36, 37). It is refreshing to see that CBT-I can capitalise on the reciprocality of pain-sleep relationship (38), because the bidirectionality of this relationship has largely been built on experimental evidence of negative interactions: in controlled settings in which the introduction of sleep disruptions and fragmentation in pain-free young adults result in an increase in spontaneous pain, increases in pain sensitivity, heightened inflammatory responses, and blunted pain habituation and endogenous pain inhibition (39-46). As Winston Churchill once said, "It is easier to break crockery than to mend it.”(47) Affirming the pain-relieving properties of CBT-I is definitely a significant step forward in our efforts to heal chronic pain.
References

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