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## Connecting insomnia, sleep apnoea and depression

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Insomnia and obstructive sleep apnoea (OSA) are the two most common sleep disorders. Insomnia is a known risk factor for incidence and severity of depression, recurrence of depressive episodes and even suicide.<sup>1</sup> Several studies have also shown that OSA can contribute to the development of depression.<sup>2</sup> Insomnia and OSA often co-occur, but previous research has not addressed the interactions, for example, whether this co-occurrence is associated with worse depression.

A new study by Lang *et al.*<sup>3</sup> attempts to address the insomnia/depression/OSA interactions. The investigators assessed OSA using home unattended polysomnography, insomnia using self-reported symptoms and depression using validated screening questionnaires. They examined depression across patients who presented with insomnia alone, OSA alone or both conditions, compared to those with neither insomnia nor OSA. They found that, in general, depression scale scores were lowest among those without either condition and with OSA, higher among those with insomnia and highest among those with both conditions. Thus, although OSA itself was not independently associated with depression scores in this study, when insomnia and OSA co-occurred, depression scores were higher than those with insomnia alone.

This study had limitations. First, the insomnia symptoms were not assessed using standard research diagnostic criteria or standard clinical measures used in the insomnia literature. Second, all of the depression screening questionnaires include items that assess sleep disturbance (which may overlap with insomnia symptoms), which may have inflated the strength of observed relationships between insomnia and depression scores. Third, patients were excluded if they were taking medication for anxiety or depression; as insomnia is often co-morbid with psychiatric disorders, it is not clear whether many patients with insomnia were systematically excluded from the study.

Still, this study makes an important contribution to the literature in that it extends the existing evidence linking insomnia to depression by showing that when insomnia is accompanied by OSA, depression may be worse. As estimates of the prevalence of insomnia

among OSA patients are as high as 67%,<sup>4</sup> this finding suggests that many OSA patients may be at risk of depression by virtue of the co-morbid insomnia symptoms.

There are several plausible reasons why OSA and insomnia may interact to worsen depression symptoms. One speculative mechanism is via arousal threshold. A core feature of insomnia is physiological and/or cortical hyperarousal, which likely results in a decreased arousal threshold. This decreased arousal threshold in insomnia can lead to increased difficulty initiating and maintaining sleep and worse insomnia symptoms. Low arousal threshold has also been shown to contribute to OSA severity through the increased fragmentation of sleep and destabilization of ventilatory control.<sup>5</sup> A low arousal threshold would not allow the accumulation of respiratory stimuli which activate upper airway dilator muscles and thus stabilize breathing.<sup>6</sup> Moreover, recurrent arousals from sleep could lead to ventilatory overshoots, unstable CO<sub>2</sub> levels and resulting apnoeas.<sup>7</sup> Recurrent apnoeas could result in both worse insomnia and worse OSA symptoms. Reduced arousal threshold may result in more fragmented and reduced quality of sleep, potentially leading to increased fatigue, increased difficulty concentrating and impaired regulation of emotion. More directly, cortical hyperarousal during sleep has been associated with worse depression symptoms. Depression is also associated with increased rapid eye movement (REM) sleep, a stage in which OSA is typically worst. Taken together, the hyperarousal associated with insomnia may interact with arousal threshold changes in OSA to produce worse experiences of depression (Fig. 1).

A second potential link among insomnia, OSA and depression is through worsening daytime symptoms. The presence of daytime sequelae such as fatigue, irritability and cognitive symptoms (e.g. difficulty concentrating) are part of the diagnostic criteria for insomnia disorder. These daytime symptoms are often what prompt patients to seek treatment. Daytime sleepiness, irritability, fatigue and cognitive dysfunction are also well-characterized consequences of OSA. Many studies have shown that untreated (or undertreated) OSA is associated with a wide range of daytime symptoms, potentially caused by both sleep fragmentation and intermittent hypoxia. Many of these daytime symptoms known to be related to both insomnia and OSA also reflect symptoms of depression. Specifically, fatigue, difficulty concentrating and irritability are all symptoms of depression as well. As OSA may exacerbate these symptoms as daytime consequences of sleep disruption, they may also overlap as increasing depression symptoms. Interestingly, evidence suggests that daytime symptoms of insomnia (not the sleep symptoms such as difficulty initiating and/or maintaining sleep) correlate most highly with depression.<sup>8</sup> Thus, OSA may worsen daytime symptoms of insomnia, which may drive an increased contribution of insomnia to depression.

In addition to these possible ways in which OSA, insomnia and depression may be linked, it is also worth noting that treatment of one of these conditions may impact the others. For example, although cognitive behavioural therapy for depression only minimally impacts insomnia symptoms and likely does not impact OSA symptoms, several studies have shown that cognitive behavioural therapy for insomnia (CBTI) can reduce symptoms of depression in addition to insomnia. Continuous positive airway pressure (CPAP) therapy for OSA has also been shown to improve depression symptoms.<sup>9</sup> The presence of insomnia among OSA

patients has been shown to reduce CPAP adherence, suggesting that when insomnia is present, it should be treated alongside OSA.<sup>10</sup> Of note, the use of sedative/hypnotics has been suggested as a potential therapy for apnoea, either to raise the arousal threshold or to facilitate CPAP adherence.<sup>11</sup> One might predict that patients with insomnia plus OSA may be particularly amenable to such strategies.

The study by Lang *et al.*<sup>3</sup> highlights an important feature of the interaction between insomnia and OSA—when these two common sleep disorders co-occur, this is associated with worse depression than when either condition is experienced alone. These findings are important as (i) the prevalence of insomnia among OSA patients is high, (ii) treatment for insomnia and OSA may impact each other and (iii) there are some speculative mechanistic links explaining these complex interactions which need to be further explored. Future studies should further characterize the role of mental health in OSA and discern specific mechanisms which may point the way towards future treatments. We applaud the authors on their innovative work.

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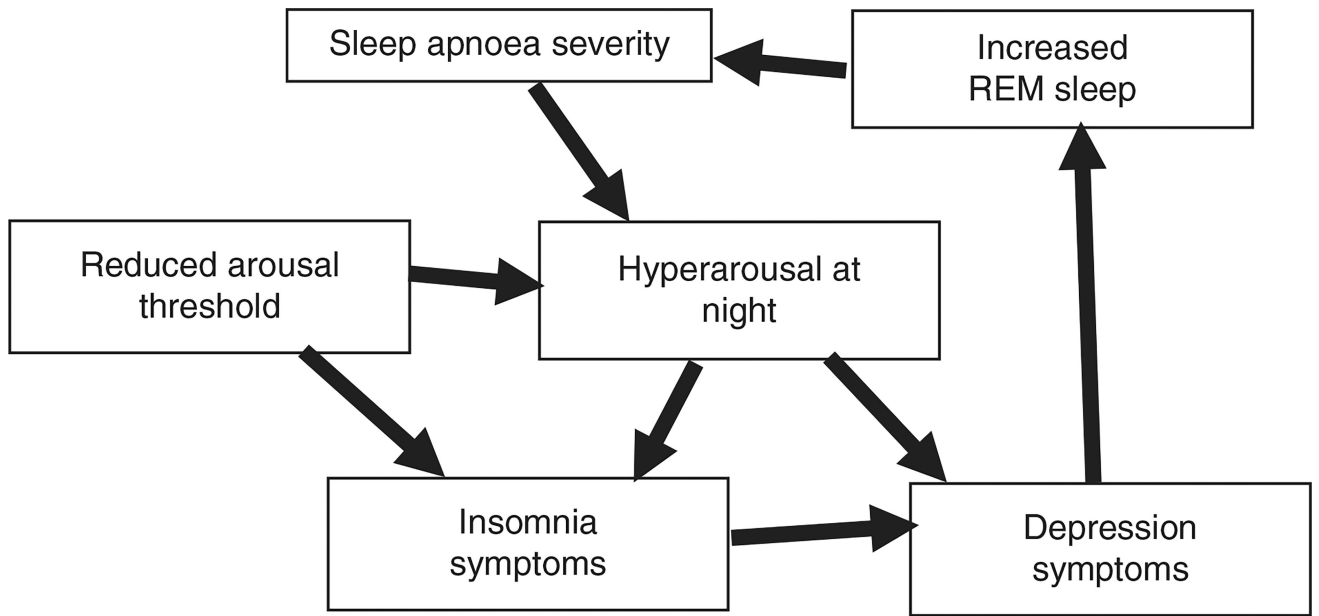
### Disclosure statement

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**Figure 1.** A potential role of arousal in sleep apnoea, insomnia and depression. REM, rapid eye movement.