COMMENTARY

Insomnia as a Predictor of Depression: Do Insomnia Subtypes Matter?

Commentary on Yokoyama et al. Association between depression and insomnia subtypes: a longitudinal study on the elderly in Japan. SLEEP 2010;33:1693-1702.

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SORTING OUT CAUSALITY IN THE RELATIONSHIP BETWEEN INSOMNIA AND DEPRESSION WAS ONCE APTLY CALLED A "CHICKEN AND EGG SITUATION."[1] Some twenty years ago Ford and Kamerow's longitudinal work highlighted the role of insomnia as a predictor of depression in this relationship.[2] Well over a dozen studies have since replicated their findings in different cohorts and over various periods of assessment. In a 2005 commentary in *SLEEP*, ("If it looks and walks like a duck…"[3]), Fred Turek considered this evidence and declared that insomnia causes depression. Not for everyone, of course, and not that insomnia always precedes or is always present in depression, but that insomnia is one independent cause of depression. It has also been pointed out that depression and insomnia are not strictly "birds of a feather,"[4] but the neurobiologic, cognitive, and behavioral features they share provide several pathways to investigate how insomnia could lead to depression. In addition, how insomnia presents (or more precisely, in what form it presents), may also be important. The epidemiologic study by Yokoyama and colleagues[5] in this issue of *SLEEP* addresses this latter end.

In their study, Yokohama et al.[5] utilize data from two time points (2003 and 2006) in the Nihon University Japanese Longitudinal Study of Ageing[6] to examine the relationship between insomnia subtypes (difficulty initiating sleep [DIS], difficulty maintaining sleep [DMS] and early morning awakening [EMA]) and the development of depression. The study provides some interesting cross-sectional data. First, there were fairly weak correlations among the three subtypes (ranging from r = 0.248 to r = 0.383), suggesting the subtypes are fairly distinct. Second, the prevalence of EMA was not more common than other subtypes in the 2003 cohort of 4,028 older adults (DIS 11.1%; DMS 22.9%; EMA 11.5%), suggesting little variation from rates observed in the general population[7] in contrast to some clinical lore that may still view EMA as distinctly related to late-life insomnia. Third, DIS was more strongly associated with depression (adjusted OR 2.02: 1.46-2.81) than EMA (1.44: 1.03-2.03) at the initial time point, while the relationship between DMS and depression was not significant. Finally, the association of any insomnia (having DIS, DMS, or EMA) to concurrent depression did not reach significance in adjusted models, suggesting there may be some added value to identifying insomnia subtypes, since in the longitudinal models reported by Yokoyama et al., only DIS at baseline predicted depression three years later.[5] Brabbins et al. had a similar finding in a smaller sample of older adults in which DIS, but not DMS or EMA, was associated with the development of new depression.[8] Notably, findings from Yokayama and colleagues are strengthened by their having controlled for sleep duration and excessive daytime sleepiness in addition to demographic and health factors.[5]

Unfortunately, the Yokoyama et al. study cannot address the concern first raised by Hohagen et al.[9] when they reported considerable variability in insomnia subtypes over time, such that the chief subtype complaint at baseline remained the chief insomnia complaint in less than 50% of patients just 4 months later. Thus, whereas insomnia was again found to relate to subsequent depression, the establishment of DIS (or any other subtype) as the putative unique phenotype underlying the insomnia-depression relationship will require more evidence. The promise of such efforts is that they may lead to both preventive medicine with respect to depression and individualized medicine with respect to presentations of insomnia. Research may proceed along a number of overlapping paths.

More specifically, longitudinal designs using diagnostic criteria for both insomnia and depression in both epidemiologic and clinical research domains can be exploited to assess: (1) not only DIS, DMS, and EMA, but also other subtypes such as insomnia, psychophysiologic insomnia, and paradoxical insomnia, or possible phenotypes associated with cognitive stance[10] or stress reactivity[11]; (2) the bi-directional relationships of insomnia and depression over multiple time points as recently accomplished by Buysse et al.[12]; and (3) the biologic (e.g., serotonergic tone, limbic hyperarousal, inflammatory markers) and psychological (e.g., response to life stressors, dysfunctional beliefs, poor coping strategies, worry/rumination) correlates of insomnia and depression.

We already have preliminary evidence that adjuvant insomnia treatments can have a greater impact on insomnia and depression than when treating the depression alone.[13,14] It remains for the current generation of insomnia-depression research to identify (if they exist) the most depression-vulnerable insomnia subtypes. Then, for such patients, ethical clinical trials need to be designed which allows us to position our existing and evolving insomnia treatments before the onset of depression to determine whether insomnia intervention can also serve as de-

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pression prevention (potentially taking out two birds with one stone, as it were).

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