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Review article

Insomnia and risk of dementia in older adults: Systematic review and meta-analysis

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ABSTRACT

There are cross-sectional evidences of an association between sleep disorders and cognitive impairment on older adults. However, there are no consensus by means of longitudinal studies data on the increased risk of developing dementia related to insomnia. We conduct a systematic review and meta-analysis to evaluate the risk of incident all-cause dementia in individuals with insomnia in population-based prospective cohort studies. Five studies of 5.242 retrieved references were included in the meta-analysis. We used the generic inverse variance method with a random effects model to calculate the pooled risk of dementia in older adults with insomnia. We assessed heterogeneity in the meta-analysis by means of the Q-test and I2 index. Study quality was assessed with the Newcastle–Ottawa Scale The results showed that Insomnia was associated with a significant risk of all-cause dementia (RR = 1.53 CI95% (1.07–2.18), z = 2.36, p = 0.02). There was evidence for significant heterogeneity in the analysis (q-value = 2.4, p < 0.001 I2 = 82%). Insomnia is associated with an increased risk for dementia. This results provide evidences that future studies should investigate dementia prevention among elderly individuals through screening and proper management of insomnia.

Contents

1. Introduction 110
2. Material and methods 110
   2.1. Search strategy 110
   2.2. Study selection 110
   2.3. Data extraction 110
   2.4. Statistical analysis 111
3. Results 111
   3.1. Synthesis of the results 113
4. Discussion 114
   Funding 114
   Conflict of interest 114
   Acknowledgment 115
   Supplementary data 115
   References 115

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1. Introduction

Studies from several countries using both cross-sectional and longitudinal designs demonstrate that self-reported insomnia complaints are common among older adults, with prevalence of 30%–60% (Buysse, 2011; Lichstein et al., 2011; Liu and Liu, 2005). Chronic insomnia is also common, ranging from 12% to 41% (Crowley, 2011; Liu and Liu, 2005).

Insomnia can occur as a symptom, a disorder, or both. Insomnia complaints associated with another medical conditions (e.g., psychiatric disorders, dependence of drugs/substances) often involve into a disorder on its own right (Sarsour et al., 2010). Insomnia as a disorder is heterogeneous, since it has varying durations, types, and etiologies. The duration include acute (three times a week for at least three months) and chronic (six months or more). Types include sleep-onset insomnia, sleep-maintenance insomnia, early morning awakening, or some combination of these, with the perception of a nonrestorative sleep and worse sleep quality. Sleep difficulty occurs despite adequate opportunity and circumstances for sleep. Etiologic categories include primary insomnia and insomnia comorbid with another condition (ICSD-2).

Previous studies showed that insomniacs presented hypometabolism in bilateral prefrontal, left superior temporal, parietal and occipital cortices, the thalamus, hypothalamus and brainstem reticular formation during wakefulness (Nofzinger et al., 2015; Harvey, 2002). On the other hand, some of these areas showed increased brain metabolism during sleep (Nofzinger et al., 2015). These areas are responsible for general arousal system, regulation of emotional processes, and cognitive performance (Bastien, 2011). Thus, these functional studies provide a neurobiological basis for the high frequency of sleep problems in psychiatric disorders, as well as the negative health consequences related to insomnia like poorer cognitive performance and increased risk of incident psychiatric disorders, as depression and dementia (Bastien, 2011; Faubel et al., 2009; Gamaldo et al., 2010; Wilckens et al., 2012).

The different sleep disorders, including insomnia, may be a consequence of brain's pathological involvement on each type of neurodegenerative disease that causes dementia. One example is how the frequency of REM sleep behavior disorder (RBD) among subjects with the synucleinopathies as multiple system atrophy (MSA), Parkinson's disease (PD), and dementia with Lewy bodies (DLB) occurs in disproportionally greater frequency than in subjects with nonsynucleinopathies neurodegenetrative diseases as Alzheimer's disease (AD) or frontotemporal dementia (FTD) (Boeve et al., 2001). On the other hand, insomnia is associated with cognitive impairment in a broad range of cognitive domains, including working memory, episodic memory, and of executive functioning. Moreover, insomnia is related to accelerated cognitive decline over 3 years (Elwood et al., 2010). However, the relationship of insomnia and the risk of dementia is still poorly understood and may be significantly confounded by other factors such as long-term benzodiazepine use, co-occurring medical and psychiatric disorders (e.g. diabetes, major depression) that are common in insomnia patients and well-known risk factors for dementia (Diniz et al., 2013; Hayden et al., 2006; Vgontzas et al., 2009a,b). Therefore, our aim was to carry out a systematic review and meta-analysis of population-based, prospective cohort studies, to evaluate the pooled risk of incident all-cause dementia, in individuals experiencing a insomnia. We hypothesized that insomnia increases the risk of all-cause dementia.

2. Material and methods

2.1. Search strategy

The systematic review and meta-analysis was carried out based on the PRISMA guidelines (Moher et al., 2009). We conducted a comprehensive search for potentially relevant studies of insomnia and dementia risk in the electronic bibliographic databases PubMed, Scopus and PsycInfo. There were no time or language limits for the searches. We also searched references of selected publications, in particular of previous systematic reviews and meta-analyses, for additional potentially relevant studies. The literature search was conducted until January 31, 2015. There were no restrictions related to publication dates.

Searches for Pubmed included the following terms: incidence (as a Medical Subject Heading – MeSH – term) OR cohort studies (MeSH). Results of the searches were combined with sets created with insomnia OR insomnia complaints AND dementia OR dementing OR Alzheimer disease OR Vascular Dementia OR Parkinson Disease OR Frontotemporal dementia OR Lewy body dementia. In the PsycInfo and Scopus, the searches used all fields to the terms: insomnia and dementia or dementing; insomnia and Alzheimer disease OR Vascular Dementia OR Parkinson Disease OR Frontotemporal dementia OR Lewy body dementia. This search retrieved a total of 5242 references.

2.2. Study selection

After reviewing the references, we selected the studies for data extraction and analysis based on the following criteria: (a) community-based prospective cohort studies; (b) age over 60 years; (c) be a population based study involving risk measures of insomnia for dementia and cognitive impairment; (d) include sufficient information to extract risk measure (odds ratio or hazard ratio and its 95% CI for the risk of dementia (all cause), and/or Alzheimer's disease and/or Parkinson's disease and/or Vascular dementia and/or Frontotemporal dementia and/or Lewy body dementia in participants with insomnia or insomnia complaints as compared with participants without insomnia; (e) information on incidence of dementia (all cause) and/or Alzheimer's disease and/or Parkinson's disease and/or vascular dementia and/or Frontotemporal dementia and/or Lewy body dementia; (f) be a study with baseline assessment and have absence of dementia.

2.3. Data extraction

We extracted the following information for the selected studies: demographic information, insomnia assessment procedures and diagnosis criteria, covariates used in the statistical models, individual studies effect sizes.

Two investigators (K.M.A. and M.V.C.) independently reviewed the title and abstract of each article retrieved from the literature search to identify potentially relevant studies. The selected articles were revised to verify whether they fulfilled the inclusion criteria for data extraction. If there was any disagreement in study selection, a third investigator (B.S.D.) made the final decision on the inclusion of the selected article. If different publications reported data from the same population, we included data from the publication with the larger sample size.

Data was extracted by two independent investigators (K.M.A. and M.C.V) using a standardized data extraction form. The following data were extracted for each study: year of publication, country, study design, depression assessment method, demographic variables, sample size and mean and standard deviation, or median and interquartile range, for each analyte. When the