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Gender Role in Sleep Disturbances among Older Adults with Traumatic Brain Injury

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Abstract

Introduction—Older adults are particularly vulnerable to poor long term outcomes and the rate of TBI in this group is increasing. Studies have shown females experience worse outcome from TBI than males, however this research has been limited. The aim of this study is to examine gender effects on the frequency of sleep disturbances in older adults post TBI.

Methods—An analysis was conducted on data obtained from the National Alzheimer's Coordinating Center (NACC) Uniform Data Set. A total of 405 patients greater than 60 years of age were examined. Sleep disturbances were measured using the Nighttime Behavioural Disturbances domain of the Neuropsychiatric Inventory – Questionnaire (NPI-Q)

Results—A significant difference ($p=0.025$) in reported sleep disturbance was identified in the female TBI population relative to the female non-TBI population. In the male No TBI group,

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Disclosure of Interest

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14.8% (n=12) experienced nighttime disturbances while those with TBI experienced 19.8% (n=17). This difference was not significant ($p=0.305$).

Conclusion—These results suggest there is a greater impact from traumatic brain injury on sleep disturbances in older females than males. Further research examining gender differences in older adults related to neuropsychiatric outcomes of TBI should be considered given the implications for treatment.

Keywords

Traumatic Brain Injury (TBI); Gender; Older Adult; Sleep Disturbance

Introduction

Brain trauma is one of the main causes of death and disability worldwide. It is estimated by the World Health Organization that Traumatic Brain Injury (TBI) will surpass many diseases as the major cause of death and disability by 2020. In the United States, an estimated 1.6 – 3 million TBI's occur each year (Viola-Saltzman, 2012). The most common causes of TBI are falls, motor vehicle accidents, and assaults (Rutland – Brown, Langlois et al, 2006). TBI is defined as “an alteration in brain functioning or brain pathology caused by an external force such as blunt trauma or penetrating objects.” (Rao, Neubauer, Vaishnavi 2015). It can be classified on a severity level using the Glasgow Coma Scale which rates the level of consciousness after a traumatic head injury. The ratings from this widely used scale classify the TBI into Mild (Score= 13–15), Moderate (Score=9–12) or Severe (8) based on various symptoms and outcomes surrounding the TBI. Symptoms may be experienced directly post TBI or several months after, and continue for years. Cognitive, emotional, behavioral and physical symptoms may result from TBI, affecting one's quality of life. One of the most common outcomes of traumatic brain injury is sleep impairment. Sleep disturbances and disorders can continue long term post TBI and impair the brain's ability to repair and recover from an injury (Wickwire et al. 2016).

The differences in outcomes post TBI based on gender and age have not been well documented. Some studies have shown that outcomes for older adults post TBI are significantly worse in terms of mortality and disability than in younger persons (Krishnamoorthy et al. 2015). Outcomes from traumatic brain injury were shown to be worse in females than in males of all ages for a variety of post TBI symptoms (Dick, R.2009; Farace & Alves, 2000). Other studies have shown poor outcomes associated with both older age and female gender (King 2014). Sleep disturbance in particular is one of the most common outcomes of TBI in the general population and the least studied (Orff, Ayalon, Drummond, 2009). In recent years, the rates of TBI have increased in older adults and falls are considered to be the major contributor (Krishnamoorthy et al. 2015). Pre-existing health issues due to aging, poor muscle strength, gait disturbances, balance issues, specific medication interactions, polypharmacy and vision impairment are known risk factors for falls in the older adults (Yi and Dams-O'Connor, 2013). Sixty percent of the TBI's diagnosed in emergency department visits in the United States in adults over 65 years of age were caused by falls (Faul et al. 2010). This is of some concern because older adults are at risk of falling during activities of daily living and may sustain a TBI from a relatively

minor fall. This was noted in a review of risk factors and mechanisms predisposing older adults to sustain TBI. Kirshnamoorthy et al.(2015) further state that outcomes for older adults following mild TBI's are significantly worse resulting in functional disability or death. In a systematic review of correlational studies examining the relationship between persistent symptoms post TBI and age, King (2014) found that 75% of the studies showed a positive relationship between older age and poorer long term outcomes. Evidence from King's (2014) systematic review confirmed older age was a strong vulnerability factor for permanent symptoms post TBI. This is important evidence for healthcare clinicians in addressing fall prevention as a strategy for managing the long term well-being of an aging population.

One of the most common outcomes of traumatic brain injury is sleep impairment. (Mathias, Alvaro, 2012). Sleep disturbances have been measured and described using a variety of methodologies in the general population and post TBI groups. Mathias and Alvaro (2012) completed a meta-analysis of 21 studies looking at the prevalence of sleep disturbances, sleep disorders such as insomnia and sleep problems such as nightmares or early morning awakening. The meta-analysis found that the prevalence of sleep disturbances following TBI, although variable, were more common than the general population. In four studies comparing overall numbers of sleep disturbances for TBI and control groups, the post TBI groups experienced significantly more problems than the control group without TBI. When large scale samples were compared, the TBI group experienced significantly more sleep disturbances, diagnosed sleep disorders, sleep apnea, snoring and nightmares than the control group. (Mathias, 2012) Individuals post-TBI were 2–4 times more likely to experience a sleep problem such as nightmares, sleep walking and early awakening than the general population. This may be the result of damage to sleep wake mechanisms.

Depending on which parts of the brain are damaged, outcomes may differ. TBI can create shearing forces in the brain which can lead to damage of many internal structures of the brain and changes to cerebral blood flow. Structures commonly damaged from TBI such as the septum pellucidum, corpus callosum, dorso-lateral pons, and midbrain all have a close relation to the brains "sleep-wake" centers (Verma, A). The autonomic nervous system (ANS) contributes to the regulation of cerebral perfusion and it has been suggested that traumatic brain injuries likely cause damage to the ANS which may contribute to the symptoms associated with TBI such as sleep disruption (Pertab et al., 2018).

Disrupted sleep has a prolonging effect on rehabilitation time which may threaten the recovery and well-being of the individual. A study done by Kalmbach et al. (2018) investigated the effect of reduced sleep on the recovery time of TBI. Functional impairments were found to be most prevalent in those who suffered from insomnia and short sleep symptoms. It was observed that subjects who had these disturbances in their sleep were up to 54% more likely to experience functional impairment. Individuals may take longer to get back into their normal routines and activities pre-TBI, leading to a decrease in quality of life overall. (Mathias, 2012). Sleep disturbances can undermine the brain recovery process and contribute to the exacerbation of other symptoms such as fatigue, depression, pain and anxiety associated with TBI (Ouellet et al., 2004; Zeitzer et al., 2009).

While two-thirds of the 1.7 million people affected by TBI each year in the United States are males, the number of females with TBI is increasing. Research focusing on the difference in gender outcomes post TBI between males and females has begun to emerge. One of the first major studies done on TBI and gender was a meta-analysis done by Farace & Alves (2000). They found that the outcome of traumatic brain injury was worse in females than males for 85 percent of the variables measured. Examples of variables found to be worse in the female population included: mortality, length of hospitalization, dizziness, fatigue, impaired concentration, insomnia, anxiety, depression, and headaches. A retrospective study done in 2016 supported these findings concluding that female patients reported significantly higher percentages than males in manifesting symptoms and mortality (Munivenkatappa, 2016). This study also found etiological differences on the brain between genders. CT scans were analyzed for abnormal findings between groups concluding that in the older adult population, females who had suffered severe TBI had a higher percentage of abnormal CT readings than their male counterparts (Munivenkatappa, 2016). There is significant evidence from King's (2014) systematic review that female gender is a vulnerability factor along with older age for permanent symptoms after sustaining mild head injuries. King (2014) stated that 50% of the correlational studies investigating female gender and longer term outcomes found a positive relationship between the two. While there is limited research examining gender differences post TBI, Hibbard et al.(1998) found female gender and older age were significant predictors of sleep difficulties almost 10 years later.

The purpose of this study is to examine the effect of gender on sleep disturbance as an outcome of traumatic brain injury in the older adult population. Female gender and increased age have been identified as high risk for prolonged symptoms post traumatic brain injury (Chiang et al. 2016). It is important to understand gender based differences in older adults with regard to sleep disturbances post TBI as they are a common outcome and have the potential to interfere with effective treatment interventions and successful recovery. Additionally, as some previous studies discussed above showed that women have poorer outcomes from TBI than men (Farace & Alves, 2000; Munivenkatappa, 2016), and subjects with TBI experienced more sleep disturbances than subjects with no TBI (Mathius, 2012). We predict in our study, TBI will have a greater effect on sleep disturbances in females than in males in the older adult population.

Methods

Data on 405 patients over 60 years of age were extracted from the National Alzheimer's Coordinating Center (NACC). NACC is responsible for the collection and storing of information gathered from 29 Alzheimer's disease centers (ADC). NACC implemented the Uniform Data Set (UDS) by developing data collection forms for initial and follow-up visits based on Clinical Task Force definitions, and made the system available to researchers (Beekley, 2007). This analysis used data from multiple ADC's. Two hundred and three patients who suffered from mild to severe traumatic brain injury were in the first group analyzed (TBI). Patients in the study were on average 3.7 years post TBI. Clinician diagnosis of TBI was used as advised by the NACC Researchers Data Dictionary (RDD) as other TBI variables rely mainly on subject and co-participant report. The TBI group included 117 females (Age= 77.2[5]) and 86 males (Age=76.7[2.1]). Male and female

patients with positive history of TBI were compared with gender matched control groups who did not experience TBI (No TBI). The control groups were matched with the TBI group for gender and age while ensuring the patients selected were as random as possible. The matching process was done with the data analysis program R, which helped to create a random matched sample. The control group included 202 patients total, 117 females (Age=77.2[7.7]) and 85 males (76.7[8.8]), falling under the same inclusionary criteria as the TBI group. It should be noted that the average cognitive test scores for both the TBI group and the no TBI group were within the normal range. Although it is possible an individual could have MCI and be included in the average score. Knowing that there are no conditions such as mild cognitive impairment (MCI) based on cognitive testing scores, reduces the potential for external factors influencing the results of this study. Inclusion and exclusion variables were set to limit confounders. Patients with co-morbidities of drug addiction, major stroke, alcohol abuse, HIV, severe psychosis, major psychiatric disorders and Alzheimer's Disease were excluded. Patients with less than a Grade 9 education were also excluded.

Measures

The Neuropsychiatric Inventory –Questionnaire (NPI-Q)

The Neuropsychiatric Inventory – Questionnaire (NPI-Q) was used in this study to measure night time sleep disturbances in the samples of post TBI and no TBI. The instrument is a self-administered questionnaire developed by Kaufer et al. (2000) that measures the severity and care giver distress of sleep disturbances. Sleep is one of the 12 neuropsychiatric symptoms measured in patients with dementia or Alzheimer's Disease. Questions related to specific behaviors associated with nighttime sleep disturbances are answered using a 3 point scale (1-mild, 2-moderate, 3-severe) and a 5 point scale measuring caregiver distress. The NPI-Q was revised for use in the clinical setting from a well-established instrument, the Neuropsychiatric Inventory (NPI). The NPI-Q has good psychometric properties and is a reliable tool to measure neuropsychiatric symptoms including sleep disturbances (Musa et al. 2017).

Statistical Analysis

Descriptive statistics were generated using R 3.6.0 statistical software. Group differences by gender were calculated using the Chi-square statistic for dichotomous variables. Significance for differences was set at $p < 0.05$ in order to achieve the highest precision possible for the study.

Results

Three hundred and ninety-three patients over the age of 60 were included in the analysis. We examined 171 males and 222 females (Total=393) with reported information regarding sleep disturbance. Demographic characteristics are reported in Table 1. The female group was first statistically analyzed comparing the prevalence of sleep disturbance between the No TBI and TBI sub groups. A statistically significant increase ($p=0.024$) of reported sleep disturbance was identified between the female groups. 9.6% ($n=10$) of females with no TBI

reported having experienced sleep disturbance, while sleep disturbance was seen in 21.7% (n=24) of females with TBI. In the male no TBI group, 14.8% (n=12) experienced nighttime sleep disturbances. This was in contrast to the TBI group which reported 19.8% (n=17). The difference between groups in the male population was not significant (p=0.305). The TBI group had an average MMSE score of 29.1 [0] and an average MOCA score of 26.6 [2.8] which both show no significant cognitive impairment. The no TBI group had a MMSE average of 28.4 [5.6] and a MOCA average of 28.3 [1.4], also in the normal range.

Discussion

The purpose of this study was to examine gender differences in the frequency of sleep disturbances among older adults with a history of traumatic brain injury. An analysis was conducted from a larger national data set of the National Alzheimer's Coordination Center (NACC). Gender differences in older adults post TBI were compared with a control group of older adults who had not experienced a TBI. Sample characteristics for both groups were the same. Both male and female groups were similar in age and had the same years of education. Cognitive scores for both groups were within the normal range. The presence of sleep disturbances were examined in both groups. Males with or without a traumatic brain injury had a similar frequency of sleep disturbances but no statistically significant difference post TBI. Males did however, report an increase in problems sleeping post TBI then males with no TBI (5% increase). Females showed a statistically significant increase in reported sleep disturbances after a TBI than with no TBI, (12.1% increase) consistent with our prediction. These results show a significantly greater impact on sleep disturbances in females after suffering a TBI. Farace & Alves (2000) suggest that gender may be an important determinant of TBI outcomes and the worst outcomes are demonstrated in women after TBI overall.

Other research showing women are more likely to have poorer outcomes after TBI compared with men (Farace & Alves, 2000; Colantonio et al., 2010) suggest that while sleep disturbances are reported in both male and females post TBI, there is a wide range of sleep disturbances which may be complicated by other factors potentially confounding results. Preexisting conditions such as anxiety or a psychiatric history may be associated with sleep problems prior to a head injury and may contribute to the persistence of sleep disturbances post TBI (Iverson et al., 2015; Ponsford et al. 2012). Further research examining gender similarities and differences in regards to TBI outcomes may be beneficial to the future of rehabilitation post TBI.

Study Limitations

One of the limitations of the study was the use of a questionnaire dependent upon caregiver report to determine the presence and severity of the sleep disturbance symptom. Caregivers analyzing the patients may perceive sleep disturbance differently or be more sensitive to what is considered a sleep disturbance. This potential variance in perception of symptomology may lead to different severity between patients. Another potential limiting factor could be that while the actual diagnosis of TBI was used, other neuropsychiatric symptoms may have confounded the presence of sleep problems as assessed by the

caregiver. Potential factors may include medication that was prescribed post TBI, or previous undiagnosed psychiatric disorders such as anxiety or depression. These have the potential to have an effect on the sleep behavior of the individuals. In addition, there may have been preexisting sleep disorders before the TBI that may have gone undiagnosed. Further research needs to be completed in this area.

Implications for Clinical Practice

It is important for clinicians to understand sleep disturbance and the complex relationship with Traumatic brain injury. Pre morbid factors can affect sleep disturbance in individuals who suffer a TBI making it difficult to target the main cause of the disturbance. It is important to develop a structured approach to diagnosing the main cause of the symptomology. This may help aid in the treatment and of sleep disturbance post TBI.

Conclusion

The findings of the study showed that older adult females with a traumatic brain injury are more likely to experience sleep disturbances than those with no history of brain injury. Older adult males experience sleep disturbances with similar frequency with or without sustaining a TBI. It should be noted that there was a greater increase in reported sleep disturbances between the female groups (12.1%) than seen between the male groups (5.0%). These results are consistent with the literature on sleep disturbance as a common outcome of TBI in older adults and supports recent findings of significant gender differences in outcomes post TBI. Persistent lack of sleep can contribute to chronic fatigue and exacerbate other symptoms post TBI, thus affecting the success of treatment and recovery. Sleep disturbances occur post TBI significantly more frequently than in the general population (Mathias and Alvaro, 2012) and outcomes are significantly worse in the older adult. (Krishnmoorthy et al. 2015). Thirty to seventy per cent of individuals suffering from TBI report disturbance in their sleep patterns which are higher rates than those reported in the general population (Ouellete et al. 2004). Information we gain from this study may help inform clinicians with evidence to assess and develop individual treatment plans for the older adult female related to sleep disturbances which may support timely resolution of symptoms.

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Recommendations for Future Research

Future research examining gender differences in the older adult post TBI with regard to sleep disturbances would contribute to the understanding of this symptom and the effect it has on the functional abilities and quality of life of female older adults post TBI. Specifically, a longitudinal study evaluating post TBI sleep disturbances for older adults at specific points in time. This information would be useful for clinicians in understanding the impact of TBI on both male and female older adults over time, and help to develop appropriate clinical interventions during the acute and chronic phase. An area for future research may include examining other sex related variables such as hormones, metabolism and brain physiology which may lead to poorer outcomes.

Table 1

Mean Demographics Characteristics and Cognitive Assessment Scores

Characteristic	TBI Group		Non TBI Group	
	<i>Males (SD)</i>	<i>Females (SD)</i>	<i>Males (SD)</i>	<i>Females (SD)</i>
Age	76.7 (2.1)	77.2 (5)	76.7 (8.8)	77.2 (7.7)
Education	16.2 (2.8)	15.5 (2.8)	15.8 (2.8)	15.5 (3.5)
MOCA Score	25 (7)	27.5 (7)	26.7 (2.8)	29.2 (1.4)
MMSE Score	29.1 (0.7)	28.8 (0.7)	27.4 (12)	29 (5.6)

Table 2

Percentage of Individuals experiencing Sleep Disturbances

	% Non TBI Patients with Sleep Disturbance (n)	% TBI Patients with Sleep Disturbance (n)	P Value
Females (n=222)	9.6% (10)	21.7% (24)	0.024
Males (n=171)	14.8% (12)	19.8% (17)	0.305