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Research paper

Risk for developing dementia among patients with posttraumatic stress disorder: A nationwide longitudinal study

Tsung-Yang Wang [a,b,e,1], Han-Ting Wei [b,f,1], Ying-Jay Liou [a,b], Tung-Ping Su [a,b], Ya-Mei Bai [a,b], Shih-Jen Tsai [a,b], Albert C. Yang [a,b], Tzeng-Ji Chen [c,d], Chia-Fen Tsai [a,b,*], Mu-Hong Chen [a,b,*]

[a] Department of Psychiatry, Taipei Veterans General Hospital, Taipei, Taiwan
[b] Department of Psychiatry, College of Medicine, National Yang-Ming University, Taipei, Taiwan
[c] Department of Family Medicine, Taipei Veterans General Hospital, Taipei, Taiwan
[d] Institute of Hospital and Health Care Administration, National Yang-Ming University, Taipei, Taiwan
[e] Department of Forensic and Neurodevelopmental Sciences, London, United Kingdom
[f] Division of Psychiatry, Kunming Branch, Taipei City Hospital, Taipei, Taiwan

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ABSTRACT

Objectives: Previous studies suggested a relationship between posttraumatic stress disorder (PTSD) in the specific population (i.e., war survivors and veterans) and subsequent dementia risk. However, whether patients with PTSD in the general population were at an increased risk for developing dementia in later life remained unclear.

Methods: The Cox regression analysis was performed using data from the Taiwan National Health Insurance Research Database. The study sample comprised 1750 patients diagnosed with PTSD between 2001 and 2009 and 7000 age-/sex-matched individuals without PTSD. Those who developed dementia during follow-up to the end of 2011 were identified.

Results: After adjusting for demographic data and medical and psychiatric comorbidities, PTSD was an independent risk factor for the risk for subsequent dementia (hazard ratio [HR]=4.37; 95% confidence interval [CI]: 2.53–7.55). There was a dose-dependent relationship between PTSD severity indicated by the frequency of psychiatric clinics visiting of PTSD (times per year) and the risk of subsequent dementia (<5: HR: 2.81, 95% CI: 1.50–5.29; 5–10: 6.90, 95% CI: 3.09–15.40; >10: HR: 18.13, 95% CI: 9.13–36.00). Furthermore, patients with depressive disorder and medical comorbidities, such as cerebrovascular diseases, diabetes mellitus, and head injuries, exhibited a higher risk for developing dementia.

Discussions: Our study suggested a significant dose-dependent association between PTSD and its severity and an increased risk of developing dementia later in life. The importance of mental care for trauma victims would increase in the coming century, and our findings broadened another era for the end result of a widely prevalent psychiatric disorder.

1. Introduction

The elderly population is currently increasing, particularly in Taiwan, where the threshold for an aging society was reached in 1993, and the elderly population will constitute more than 20% of the overall population in 2026; therefore, the number of elderly people suffering from dementia has become a major public health concern. The prevalence of dementia in Taiwanese people exceeding 65 years of age has been estimated to range between 2.0% and 4.3% (Liu et al., 1994, 1995, 1996, 1998). Several risk factors, including low intelligence, limited education (Schmand et al., 1997), substance use (Saunders et al., 1991), and cardiovascular diseases (Whitmer et al., 2005), may contribute to dementia. Trauma also played a potential role in the development of dementia in later life. Head injury was indicated as one of the risk factors associated with an increased risk of dementia (Plassman et al., 2000). The interest in psychological trauma, such as posttraumatic distress disorder (PTSD), has recently intensified.

The DSM-IV-TR defines trauma as a personal experience involving actual or threatened death or severe injury, or a threat to a person's integrity (Criterion A1), and a response involving intense fear, helplessness, or horror (Criterion A2). The DSM-5, which was published in May 2013, expands the definition of trauma, indicating that trauma can be experienced as well as witnessed or

* Corresponding authors at: Department of Psychiatry, Taipei Veterans General Hospital, Taipei 112, Taiwan.
E-mail addresses: cftsai@vghtpe.gov.tw (C.-F. Tsai), kremer7119@gmail.com (M.-H. Chen).
[1] Tsung-Yang Wang and Han-Ting Wei equally contributed to this work.

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learned (Criterion A). The DSM-IV-TR organizes PTSD symptoms into 3 categories, which must be present for at least 1 month after a traumatic event and must cause functional impairment: re-experiencing intrusions of the trauma (Criterion B), avoidance of stimuli associated with the trauma and numbing of general responsiveness (Criterion C), and hyperarousal symptoms (Criterion D) (American Psychiatric Association, 2000). An additional symptom, negative alterations in cognition and mood, has been added to the DSM-5 (Criterion D) to emphasize the link between PTSD and cognitive function (Carmassi et al., 2013).

PTSD has been proposed to be associated with an increased risk for developing dementia, mostly within the populations of veterans and war victims. The incidence and prevalence of dementia was greater in veterans with PTSD (Qureshi et al., 2010), who exhibit a nearly 2-fold higher risk for developing dementia (Yaffe et al., 2010). Dementia was diagnosed according to ICD-10 criteria in 16% of Holocaust survivors (Sperling et al., 2011). It was still unclear whether the increased risk was due to a common risk factor underlying PTSD and dementia or to PTSD being an independent risk factor for dementia.

Two mechanisms have been proposed to describe how PTSD influences dementia. The first was the direct influence of previous life traumas, which might trigger the persistent over-activation of the hypothalamic-pituitary-adrenal (HPA) axis and the adrenergic system (Taylor et al., 2009). In addition, lifetime trauma might lead to health problems independent of PTSD later in life (D'Andrea et al., 2011), which might indirectly lead to susceptibility to dementia. The second mechanism involved conceptualizing dementia as a de novo traumatic experience that could increase the rate of cognitive decline by activating a debilitating stress response or precipitating PTSD symptoms and correlates (Burnes and Burnette, 2013).

Thus, we conducted a population-based study using the Taiwan National Health Insurance Research Database (NHIRD) to examine the incidence of dementia in patients with PTSD and compared them with matched controls without PTSD. In addition, we identified independent factors for predicting incident dementia.

2. Methods

2.1. Data source

The Taiwan National Health Insurance (NHI) program was implemented in 1995 and offers comprehensive medical care coverage to all residents of Taiwan. The National Health Research Institutes (NHRI) manages the insurance claims database, the National Health Insurance Research Database (NHIRD), which consists of health care data from more than 97% of the entire Taiwanese population. The NHRI audits and releases the NHIRD for use in health service studies. Patients included in the NHIRD are anonymous to ensure that their individual privacy is maintained. The database contains comprehensive information on the insured patients, including demographic data, dates of clinical visits, and disease diagnoses. The diagnostic codes used were based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). The NHIRD has been used extensively in numerous epidemiologic studies in Taiwan (Shen et al., 2013; Wu et al., 2012; Chen et al., 2013).

2.2. Inclusion criteria for patients with PTSD and the control group

Patients exceeding 45 years of age who were diagnosed with PTSD (ICD-9-CM code: 309.81) by psychiatrists between January 1, 2001 and December 31, 2009 and who had no history of organic mental disorders or dementia (ICD-9-CM codes: 290–294, 331) before enrollment were included in the PTSD cohort. The age- and sex-matched (1:4) control cohort (non-PTSD cohort) was randomly identified after eliminating the study cases, patients who had been diagnosed with PTSD at any time, and patients with any organic mental disorder or dementia (ICD-9-CM codes: 290–294, 331) before enrollment. Dementia (ICD-9-CM codes: 290.0–290.4, 294.1–294.2, 331.0–331.2) diagnosed by psychiatrists or neurologists was identified during the follow-up (to December 31, 2011 or death). Furthermore, the dementia-related risk factors were assessed: depressive disorder, alcohol use disorders, substance use disorders, cerebrovascular diseases, hypertension, diabetes mellitus, dyslipidemia, chronic renal diseases, and head injury. All diagnoses were provided at least twice by corresponding physicians to achieve diagnostic validity. The level of urbanization (level 1 to level 5; level 1: most urbanized region; level 5: least urbanized region) was also assessed (Liu et al., 2006).

2.3. Statistical analysis

For between-group comparisons, an independent t test was used for continuous variables and Pearson's chi-squared test was used for nominal variables. The Cox regression model was used to investigate the hazard ratios (HRs) with 95% confidence intervals (CIs) for developing dementia after adjusting for demographic data and medical and psychiatric comorbidities. In addition, we performed a Cox regression analysis with an adjustment of demographic data and medical and psychiatric comorbidities to assess the relationship between PTSD severity indicated by the frequency of psychiatric clinics visiting of PTSD (times per year) and the risk of subsequent dementia. Sensitivity tests were performed to calculate the risk of dementia after excluding the first 3 years and 5 years of observation. Subanalysis stratified by sex was performed to investigate the role of sex in the likelihood of dementia. All data processing and statistical analyses were performed using the Statistical Package for Social Science (SPSS) Version 17 software (SPSS Inc.) and Statistical Analysis Software (SAS) Version 9.1 (SAS Institute, Cary, NC).

3. Results

3.1. Demographic data of the study patients

In total, 81 PTSD patients (7.54 per thousand person-years) and 54 comparison controls (1.22 per thousand person-years) developed dementia in the follow-up period (Table 1). Compared with the matched controls, PTSD patients exhibited a significantly higher prevalence of the medical and psychiatric comorbidities, including cerebrovascular disease ($p < 0.001$), hypertension ($p = 0.002$), diabetes mellitus ($p = 0.005$), dyslipidemia ($p < 0.001$), and head injury ($p < 0.001$), depressive disorder ($p < 0.001$), alcohol use disorders (< 0.001), and substance use disorders (< 0.001); significant differences were observed regarding psychosocial factors such as the level of urbanization ($p < 0.001$) and the income-related insured amount ($p < 0.001$).

3.2. Association of posttraumatic stress disorder with the development of dementia

When examining the association of PTSD with the development of dementia, patients with PTSD exhibited a 4.37-fold higher risk of developing dementia than the controls did (adjusted HR = 4.37; 95% CI: 2.53–7.55) after adjusting for demographic data and medical and psychiatric disorders (Table 2). The crude HR and 95% CI of PTSD with the risk of subsequent dementia was 6.57 and 4.66–9.27 ($p < 0.001$). The survival curve for the development of