Brain, Behavior, and Immunity 36 (2014) 176–182

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Phobic anxiety symptom scores and incidence of type 2 diabetes in US men and women ☆

Maryam S. Farvid [a,*], Lu Qi [a,d], Frank B. Hu [a,b,d], Ichiro Kawachi [c], Olivia I. Okereke [b,d,e], Laura D. Kubzansky [c], Walter C. Willett [a,b,d]

[a] Department of Nutrition, Harvard School of Public Health, Boston, MA, United States
[b] Department of Epidemiology, Harvard School of Public Health, Boston, MA, United States
[c] Department of Social and Behavioral Sciences, Harvard School of Public Health, Boston, MA, United States
[d] Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, United States
[e] Department of Psychiatry, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, United States

ARTICLE INFO

Article history:
Received 6 August 2013
Received in revised form 24 October 2013
Accepted 25 October 2013
Available online 31 October 2013

Keywords:
Phobic anxiety
Type 2 diabetes

ABSTRACT

Context: Emotional stress may be a risk factor for type 2 diabetes (T2D), but the relation between phobic anxiety symptoms and risk of T2D is uncertain.
Objective: To evaluate prospectively the association between phobic anxiety symptoms and incident T2D in three cohorts of US men and women.
Design, setting and patients: We followed 30,791 men in the Health Professional's Follow-Up Study (HPFS) (1988–2008), 68,904 women in the Nurses' Health Study (NHS) (1988–2008), and 79,960 women in the Nurses' Health Study II (NHS II) (1993–2011). Phobic anxiety symptom scores, as measured by the Crown–Crisp index (CCI), calculated from 8 questions, were administered at baseline and updated in 2004 for NHS, in 2005 for NHS II, and in 2000 for HPFS. Incident T2D was confirmed by a validated supplementary questionnaire. We used Cox proportional hazards analysis to evaluate associations with incident T2D.
Results: During 3,099,651 person-years of follow-up, we documented 12,831 incident T2D cases. In multivariate Cox proportional-hazards models with adjustment for major lifestyle and dietary risk factors, the hazard ratios (HRs) of T2D across categories of increasing levels of CCI (scores = 2 to <3, 3 to <4, 4 to <6, ⩾6), compared with a score of <2, were increased significantly by 6%, 10%, 10% and 13% (P_{trend} = 0.001) for NHS; and by 19%, 11%, 21%, and 29% (P_{trend} < 0.0001) for NHS II. Each score increment in CCI was associated with 2% higher risk of T2D in NHS (HRs, 1.02, 95% confidence intervals: 1.01–1.03) and 4% higher risk of T2D in NHS II (HRs, 1.04, 95% confidence intervals: 1.02–1.05). Further adjustment for depression did not change the results. In HPFS, the association between CCI and T2D was not significant after adjusting for lifestyle variables.
Conclusion: Our results suggest that higher phobic anxiety symptoms are associated with an increased risk of T2D in women.

1. Introduction

The prevalence of type 2 diabetes (T2D) is increasing at alarming rates in the US and worldwide (Chen et al., 2011; Zabetian et al., 2013). In addition to well-known diabetic risk factors such as diet, obesity, physical inactivity, age, race, and a family history of T2D (Psaltopoulou et al., 2010; Venables and Jeukendrup, 2009), recent studies have suggested a role of emotional stress in the etiology of T2D (Kato et al., 2009; Pouwer et al., 2010; Rod et al., 2009). The epidemiological studies support the concept that different forms of emotional stress, particularly depression, general emotional stress, anxiety, anger, hostility and sleeping problems (Pouwer et al., 2010), contribute to an elevated risk of T2D. Anxiety disorders are the most prevalent mental disorders and lifetime prevalence of either specific phobia or social phobia is over 12% in the U.S. (Kessler et al., 2005a,b).

Emotional stress may influence behavioral factors and thereby increase the risk of T2D through unhealthy dietary intake, excessive alcohol consumption, smoking and low exercise levels (Rod et al., 2009; Kye and Park, 2012; Bonnet et al., 2005). Additional evidence also suggests the association between phobic anxiety symptoms and increasing inflammatory biomarkers such as C-reactive protein, tumor necrosis factor α, leptin, soluble E-selectin

☆ Funding sources had no role in the design or analysis of the study or the decision to submit the manuscript for publication.
* Corresponding author.
E-mail address: mfarvid@hsph.harvard.edu (M.S. Farvid).

0889-1591/$ - see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.bbi.2013.10.025

and soluble intercellular adhesion molecule (Brennan et al., 2009; Pitsavos et al., 2006), which are well-known risk factors for T2D (Mirza et al., 2012). Importantly, phobic anxiety is treatable; thus, any potential impacts on T2D incidence may be amendable through early identification and intervention.

An association between phobic anxiety symptoms and increased risk of coronary heart disease (CHD) in men and women has been previously reported in our and other cohorts (Albert et al., 2005; Kawachi et al., 1994; Watkins et al., 2010), to date, however, the relationship between phobic anxiety symptoms and T2D incidence has not been directly examined. Therefore, using data from three prospective cohorts, the Nurses' Health Study (NHS), Nurses' Health Study II (NHS II) and Health Professional's Follow-up Study (HPFS), we examined the association between phobic anxiety symptom scores, as measured by Crown–Crisp index (CCI), and T2D incidence in women and men.

2. Research design and methods

2.1. Study population

We used data from 3 prospective cohort studies: NHS (started in 1976; $n = 121,704$; age ranged at baseline: 30–55 years; enrolled from 11 US states), NHS II (established in 1989; $n = 116,643$; age ranged at baseline: 24–43 years; enrolled from 14 US states) and HPFS (initiated in 1986; $n = 51,529$; age ranged at baseline: 40–75 years; enrolled from 50 US states). In all the 3 cohorts, questionnaires were administered at baseline and biennially thereafter to collect and update information on lifestyle practices and occurrence of chronic diseases. Information on phobic anxiety symptoms was first obtained on the 1988 questionnaire in NHS ($n = 103,614$), on the 1993 questionnaire in NHS II ($n = 87,238$) and on the 1988 questionnaire in HPFS ($n = 48,834$); this served as the baseline populations for our analyses. Participants were excluded if they had T2D, cancer, CHD or stroke at baseline ($n = 16,255$ in NHS, $n = 5935$ in NHS II and $n = 7354$ in HPFS), missing information on T2D diagnosis date ($n = 3355$ in NHS, $n = 937$ in NHS II, and $n = 1524$ in HPFS), age ($n = 48$ in NHS and $n = 182$ in NHS II), or phobic anxiety symptom score data ($n = 15,052$ in NHS, $n = 224$ in NHS II, and $n = 9165$ in HPFS). After exclusions, data from 68,904 women in NHS, 79,960 women in NHS II and 30,791 men in HPFS were available for the analysis. The study protocol was approved by the institutional review boards of Brigham and Women's Hospital and Harvard School of Public Health (Boston, Massachusetts, United States).

2.2. Assessment of T2D

In the three cohorts, participants who reported a new diagnosis of T2D on any of the biennial questionnaires were sent supplementary questionnaires regarding symptoms, diagnostic tests, and hypoglycemic therapy. A case of T2D was confirmed if at least one of the following items was reported on the supplementary questionnaire according to the National Diabetes Data Group criteria (National Diabetes Data Group, 1979): (1) one or more classic symptoms (excessive thirst, polyuria or frequent urination, weight loss, or hunger) plus fasting plasma glucose concentrations $\geqslant$140 mg/dl or random plasma glucose concentrations $\geqslant$200 mg/dl; (2) $\geqslant$2 elevated plasma glucose concentrations on different occasions (fasting concentrations $\geqslant$140 mg/dl, random plasma glucose concentrations $\geqslant$200 mg/dl, and/or concentrations $\geqslant$200 mg/dl after $\geqslant$2 h shown by oral glucose tolerance testing) in the absence of symptoms; or (3) treatment with hypoglycemic medication (insulin or oral hypoglycemic agent). For cases diagnosed in 1998 and later, the fasting plasma glucose threshold was lowered to 126 mg/dl according to the American Diabetes Association criteria (Gavin et al., 1997). The validity of the supplementary questionnaire has been demonstrated previously in the NHS (Manson et al., 1991; Field et al., 2001). Only cases confirmed by the supplemental questionnaires were included in the current analysis.

2.3. Assessment of phobic anxiety symptom scores: the Crown–Crisp index (CCI)

The phobic anxiety scale of the CCI measures personality symptoms of phobic anxiety (Crown and Crisp, 1966). It is a standardized, self-rating inventory of 8 questions on common symptoms of phobic anxiety with two (0, 2) to three (0, 1, 2) levels of possible responses to each question. The scores range from 0 to 16, with higher scores given to higher levels of phobic anxiety symptoms (Crown and Crisp, 1966). The CCI has been validated in psychiatric outpatient clinic settings and it could discriminate patients with anxiety disorders and agoraphobia from healthy controls and patients with other forms of psychopathology (e.g., depressive, obsessive–compulsive) (Crown and Crisp, 1966; Mavissakalian and Michelson, 1981). The validity of the phobic anxiety scale of CCI in the NHS population has been tested through assessing the association with tranquilizer medication (Albert et al., 2005). For those with missing data on 1 or 2 questions, the total score was divided by the fraction of questions answered and then rounded to the nearest whole number. The CCI was completed by participants in the NHS in 1988, in NHS II in 1993 and HPFS in 1988 and updated in 2004 for NHS, in 2005 for NHSII, and in 2000 for HPFS. The Spearman correlation between CCI scores in 1988 and 2004 (NHS), 1993 and 2005 (NHS II) and 1988 and 2000 (HPFS) were high ($r = 0.75$, $p < 0.0001$ in NHS, $r = 0.70$, $p < 0.0001$ in NHS II, and $r = 0.75$, $p < 0.0001$ in HPFS), an indication that scores reliably represent long-term phobic anxiety symptom levels.

2.4. Assessment of covariates

In the biennial follow-up questionnaires, we inquired and updated information on risk factors for chronic diseases, such as body weight, cigarette smoking, physical activity, aspirin use, multivitamin use, family history of diabetes, menopausal status and postmenopausal hormone use (NHS and NHS II only), marital status and routine screening for physical exam. Dietary information (including alcohol) was assessed using a validated semi-quantitative food frequency questionnaire every 4 year starting from 1986 (NHS), 1991 (NHS II) and 1986 (HPFS) (Feskanich et al., 1993).

We calculated a diabetes dietary score composed of quintile values of polyunsaturated fat to saturated fat ratio, trans fat (inverted), cereal fiber, and glycemic load (inverted) by standardizing and summarizing the respective continuously scaled dietary variables. This method was described in detail elsewhere (Hu et al., 2001). In women, we defined depression status (yes/no) as having: Mental Health Index-5 $\leqslant$52 [from the Medical Outcomes Short Form-36, scaled from 0 to 100; higher scores indicate better mental health; included on questionnaires in 1992, 1996, and 2000 in the NHS and in 1993, 1997 and 2001 in the NHS II], self-reported regular antidepressant use, and/or self-reported physician-diagnosed depression. In men, we defined depression status (yes/no) based on self-reported regular antidepressant use and/or self-reported physician-diagnosed depression.

2.5. Statistical analyses

Person-years for each participant were calculated from the return date of the phobic anxiety questionnaire (1988 in NHS, 1993 in NHS II and 1988 in HPFS) to the date of diagnosis of