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Journal of Affective Disorders 88 (2005) 87–91

JOURNAL OF AFFECTIVE DISORDERS

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Brief report

Does generalized anxiety disorder predict coronary heart disease risk factors independently of major depressive disorder?

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Received 3 November 2004; accepted 16 May 2005
Available online 11 July 2005

Abstract

Background: Anxiety symptoms are associated with elevated coronary heart disease (CHD) risk, but it is not known whether such associations extend to anxiety disorders or if they are independent of depression. We sought to determine if generalized anxiety disorder is associated with elevated CHD risk, and whether this association is independent of or interacts with major depressive disorder.
Methods: Generalized anxiety and major depressive disorders were assessed in a cross-sectional survey of a representative sample of U.S. adults aged 25–74 ($N=3032$). Coronary heart disease risk was determined by self-reported smoking status, body mass index, and recent medication use for hypertension, hypercholesterolemia, and diabetes.
Results: Generalized anxiety disorder independently predicted increased CHD risk ($F(1,3018)=5.14$; $b=0.39$; 95% confidence interval (0.05–0.72)) and tended to denote the greatest risk in the absence of major depressive disorder.
Limitations: The cross-sectional design cannot determine the causal direction of the association.
Conclusions: Generalized anxiety disorder appears to be associated with elevated CHD risk in the general population. It may denote excess CHD risk relative to major depressive disorder, and clinicians should consider CHD risk when treating generalized anxiety disorder.

Keywords: Generalized anxiety disorder; Major depressive disorder; Coronary heart disease; Blood pressure; Smoking

1. Introduction

Coronary heart disease (CHD) is the leading cause of mortality in the United States (Arias et al., 2003) and depressive symptomatology has been implicated as a prognostic factor for the presence and course of CHD. For example, depression is associated with both incidence (Ferketich et al., 2000) and progression (Lett et al., 2004) of CHD. Anxiety disorders are similarly hypothesized to denote elevated CHD risk (Kubzansky et al., 1998), but to date few tests of this hypothesis have been reported and all but one (Weissman et al., 1990) were limited to questionnaire anxiety assessments (Haines et al., 1987; Kawachi et al.,

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doi:10.1016/j.jad.2005.05.012

1994a,b). We are unaware of any studies to date that have evaluated CHD risk among individuals with generalized anxiety disorder (GAD). Similarly, it is important to address whether anxiety disorders are independent of, or interact with comorbid major depressive disorder (MDD). Disentangling CHD risk for these often co-occurring conditions (Kessler et al., 2003) can address the criticism that studies linking anxiety with CHD merely reflect depression effects (Kubzansky et al., 1998). Finally, most studies of anxiety and CHD exclude female participants (for an exception see Eaker et al., 1992) which is undesirable because women are substantially more likely to be diagnosed with anxiety disorders.

We evaluated the association between GAD and CHD risk in a large, cross-sectional survey of a probability sample of US adults. We used an aggregate measure of established risk factors that explain the majority of CHD risk, e.g., hypertension, hypercholesterolemia, diabetes, smoking, and overweight (Greenland et al., 2003). We also tested whether GAD was associated with individual behavioral (cigarette smoking) and pathophysiological processes (hypertension) that are elevated among anxious individuals (Kubzansky et al., 1998; Hayward, 1995).The independent and joint effects of GAD with MDD were explicitly modeled in the analyses, and we included a substantial number of women ($N=1559$) in our investigation.

2. Method

We analyzed data from the National Survey of Midlife Development in the United States (MIDUS), a nationally representative telephone and postal survey of 3032 adults aged 25–74 in the continental US (Brim et al., 2000). The response rate for both assessments was approximately 60.8%. All participants consented to both surveys.

3. Measures

3.1. DSM-III-R disorders

The 12-month prevalence of GAD and MDD was measured during the phone interview using the short form of the Composite International Diagnostic Interview (CIDI-SF; Kessler et al., 1998a). The CIDI-SF is a fully structured diagnostic interview that assesses mental disorders based on DSM-III-R criteria (American Psychiatric Association, 1987). The CIDI-SF GAD and MDD assessments have good classification accuracy relative to the full CIDI instrument (99% and 93%, respectively) (Kessler et al., 1998a) and in turn, the full CIDI instrument has good agreement with clinical diagnoses (Wittchen, 1994; Kessler et al., 1998b).

3.2. CHD risk factors

The presence of CHD risk was derived from the sum of five questions regarding hypertension, smoking, high cholesterol, diabetes, and overweight. Hypertension, hypercholesterolemia, and diabetes were defined by the presence or absence of current (within the past 30 days) medication use for those conditions. Hypertension, smoking, hypercholesterolemia and diabetes account for the bulk of risk for CHD events and similar self-reports of medication use for these conditions predict mortality (Greenland et al., 2003). Body mass index (BMI) is another established CHD risk factor and we grouped participants into categories corresponding to normal weight ($BMI \leq 25$) versus overweight/obese ($BMI > 25$). These risk factors were coded in a binary fashion (0 = absent, 1 = present) and summed to create a composite CHD risk variable. We imputed to zero a small number (<1%) of missing values for CHD risk and used major demographic variables to impute missing ethnicity (2.9%), BMI (4.9%) and two values of education level. Analyses were insensitive to these imputations.

We regressed the composite CHD risk score on GAD, MDD, and their interaction, simultaneously adjusting for gender, age, education level, marital status, and ethnicity. We further evaluated whether associations between GAD and CHD risk were sensitive to the frequency of medical care seeking, defined using four questions regarding the number of medical contacts for physical health over the last 12 months (sum of routine, urgent, and scheduled visits in quartiles). A small number (3.1%) of missing values for these visits were imputed as above.

Because individuals with symptoms of anxiety and depression have higher rates of hypertension and smoking (Hayward, 1995) we disaggregated the CHD risk variable to test whether GAD independently

predicted these CHD risk factors individually. All statistical tests were two-tailed and predictors were considered significant if $p \leq 0.05$. We used the Huber/White method of variance estimation to provide robust standard error estimates (Long and Freese, 2003).

4. Results

The estimated 12-month prevalence of GAD was 3% ($N=89$; 72% female) while 14% ($N=418$; 63% female) of the population had MDD. 60 of the 89 GAD cases also had MDD (67%), and 44 (73%) of those comorbid cases were women. For the summary CHD risk variable, both GAD ($F(1,3018)=5.14$, $p<0.05$; $b=0.39$; 95% CI=0.05–0.72) and MDD ($F(1,3018)=9.02$, $p<0.01$; $b=0.14$; 95% CI=0.05–0.23) were associated with greater CHD risk. Controlling for the number of medical contacts in the last 12 months did not alter the effects observed for GAD ($b=0.34$; 95% CI=0.01–0.66, $p<0.05$). The interaction of GAD and MDD approached statistical significance ($p=0.065$) and the effect was somewhat reduced after further adjustment for medical visits ($p=0.09$). Because these joint effects are of theoretical interest (Kubzansky et al., 1998) fully adjusted means for CHD risk across these two disorders are presented on the left-hand side of Fig. 1.

Those with GAD had 3.10 times greater odds of taking blood pressure (BP) medication (95% CI=1.27–7.56; $p<0.05$) and 2.28 times greater odds of being a current smoker (95% CI=1.04–5.00; $p<0.05$). These effects persisted following adjustment for medical visits (OR=2.61; 95% CI=1.04–6.52 for BP; OR=2.29; 95% CI=1.04–5.01 for smoking). The interaction of GAD and MDD approached conventional significance levels only for recent hypertension medication use ($\chi^2=2.96$, $df=1$, $p=0.085$), although it was sensitive to adjustment for medical visits ($\chi^2=2.35$, $df=1$, $p=0.13$). Because the ordinal pattern

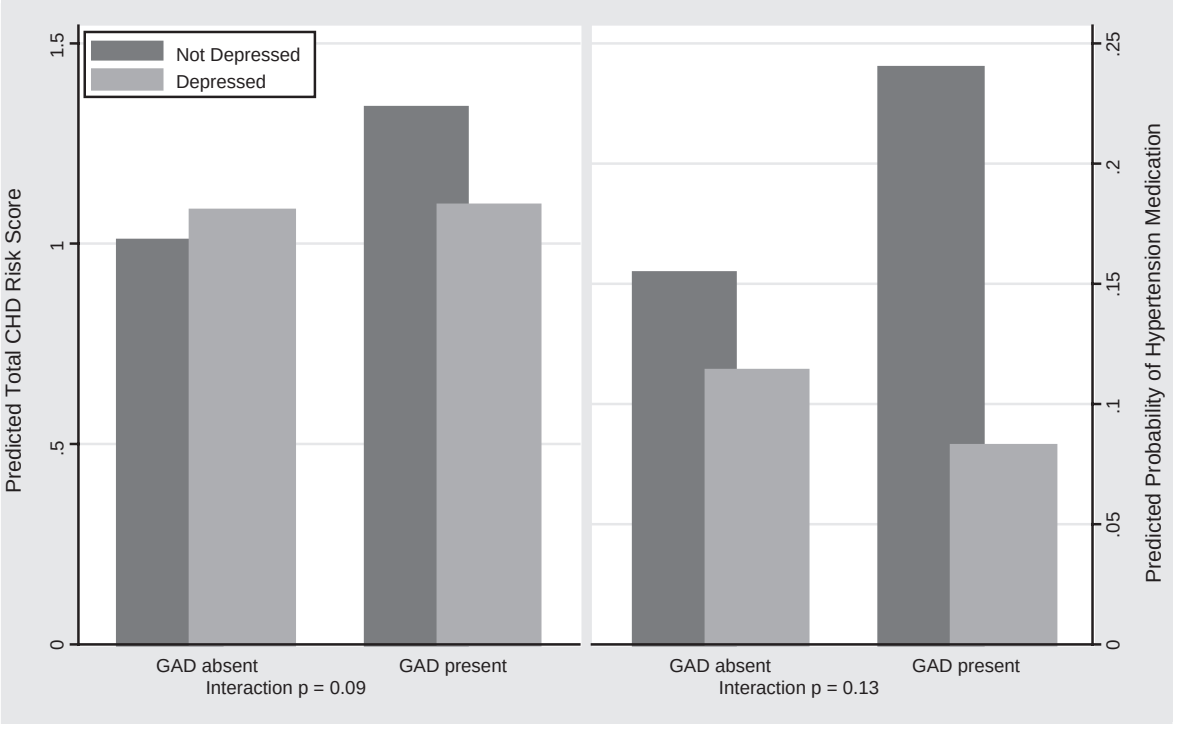

Fig. 1. Predicted total CHD risk (means) and hypertension medication use (probabilities) by generalized anxiety disorder (GAD) and major depressive disorder. Note: CHD=coronary heart disease. Predictions are adjusted for age, gender, ethnicity, education, marital status, medical visits over the last 12 months and first-order effects of generalized anxiety disorder and major depressive disorder. Total sample $N=3032$.

of hypertension risk for GAD as a function of MDD has not been described, predicted probabilities for hypertension medication use by both GAD and MDD are presented on the right side of Fig. 1. Generalized anxiety disorder and the GAD by MDD interaction were unrelated to cholesterol, BMI, and diabetes (p values >0.16).

5. Discussion

This investigation is the first to compare CHD risk among individuals diagnosed with GAD and MDD via structured interview, and to evaluate the independent and joint associations of our estimates of these disorders with CHD risk among a representative sample of US adults. This work also included a large number of women, notably absent from prior epidemiologic investigations of anxiety symptoms and CHD risk (Hayward, 1995). We found that GAD independently predicted increased CHD risk, particularly for major modifiable risk factors, i.e., smoking and hypertension. Although these risk differences were modest, they complement earlier work showing that anxiety symptoms predict self-reported CHD risk factors (Kawachi et al., 1994a) as well as subsequent CHD mortality (Kawachi et al., 1994a,b). Increased risk among GAD cases was not explained by MDD, a potent rival hypothesis given the established depression–CHD risk relation (Lett et al., 2004) and the substantial comorbidity of these disorders (Kessler et al., 2003). Moreover, the interaction patterns suggest that GAD without MDD is associated with elevated CHD risk. However, this pattern did not achieve conventional significance levels and should be interpreted accordingly.

Despite these contributions, the cross-sectional design cannot establish the causal direction of the increased CHD risk observed for GAD cases. We also relied upon reported rather than objectively verified medication use. However, such measures have established validity in terms of correspondence with CHD mortality (Greenland et al., 2003) and any misclassification would probably bias the data in favor of the null hypothesis.

It is important to replicate these findings in prospective studies using objective risk assessments. Previous work has shown higher smoking prevalence among individuals with panic disorder (McCabe et al., 2004), so further examination of the relative strength of the association between CHD risk factors and the spectrum of anxiety disorders would also be useful. Longitudinal studies could clarify whether such disorders represent an independent CHD risk marker, or if any excess CHD risk can be explained by established prognostic factors. Until such studies are undertaken, it appears prudent to consider CHD risk assessment among individuals diagnosed with generalized anxiety disorder.

Acknowledgments

This research was supported by subcontract 833F173 from Rutgers University, Institute for Health, Health Care Policy and Aging research, under grant PO1 AG020166 (Integrative Pathways to Health and Illness) from the National Institute of Aging. Portions of this research were presented at the 63rd annual meeting of the American Psychosomatic Society, Vancouver, Canada.

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