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Trait Anger But Not Anxiety Predicts Incident Type 2 Diabetes: The Multi-Ethnic Study of Atherosclerosis (MESA)

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Abstract

Objective—Prior studies have shown a bidirectional association between depression and type 2 diabetes mellitus (T2DM); however, the prospective associations of anger and anxiety with T2DM have not been established. We hypothesized that trait anger and anxiety would predict incident T2DM, independently of depressive symptoms.

Research Design and Methods—In the Multi-ethnic Study of Atherosclerosis (MESA), we prospectively examined the association of trait anger and trait anxiety (assessed via the Spielberger Trait Anger and Anxiety Scales, respectively) with incident T2DM over 11.4 years in 5,598 White, Black, Hispanic, and Chinese participants (53.2% women, mean age 61.6 years) at baseline without prevalent T2DM or cardiovascular disease. We used Cox proportional hazards models to calculate the hazard ratios (HR) of incident T2DM by previously defined anger category (low, moderate, high), and anxiety quartile, as there were no previously defined categories.

Results—High total trait anger was associated with incident T2DM (HR 1.50; 95% CI 1.08–2.07) relative to low total trait anger. The association was attenuated following adjustment for waist circumference (HR 1.32; 95% CI 0.94–1.86). Higher anger reaction was also associated with

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Dr. Abraham and Ms. Shah had full access to all data in the study and take responsibility for the integrity and accuracy of the data analysis.

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incident T2DM (HR=1.07; 95% CI 1.03–1.11) that remained significant after adjusting for potential confounders/explanatory factors. In contrast, trait anxiety did not predict incident T2DM.

Conclusions—High total trait anger and anger reaction are potential modifiable risk factors for T2DM. Further research is needed to explore the mechanisms of the anger-diabetes relationship and to develop preventive interventions.

Psychological disorders may have a direct impact on the development of the type 2 diabetes and its subsequent management, outcomes, and complications. Depression has a bidirectional relationship with type 2 diabetes mellitus (Golden et al., 2008). Certain temperaments, including anger, have been linked to cardiovascular disease risk (Williams et al., 2000; Williams et al., 2001). Only one previous study has examined whether a similar relationship exists between anger and type 2 diabetes (Golden et al., 2006). In the Atherosclerosis Risk in Communities Study (ARIC) of 11,615 participants, those rated in the highest category of trait anger temperament had a 34% increased risk of diabetes, than those in the lowest category (Golden et al., 2006). This prior study, however, lacked comprehensive data on markers of inflammation, a potential intermediary biological factor.

Anxiety is often associated with depression (Katon et al., 2007; Suls et al., 2005), and the symptoms of anxiety and depression overlap and are often measured with psychological assessment scales in patients with type 2 diabetes or those at risk for development of diabetes (Anderson et al., 2002; Grigsby et al., 2002). Previous studies have shown mixed results regarding the association between anxiety and diabetes, and few have been longitudinal studies (Engum, 2007; Fisher et al., 2008; Hall et al., 2009). A positive association between anxiety and diabetes was demonstrated in nine studies (Engum, 2007; Wu et al., 2011; Paddison et al., 2011; Khuwaja et al., 2010; Lynch et al., 2010; Collins et al., 2009; Almawi et al., 2008; Tuncay, et al., 2008; Thomas et al., 2003), but there was no significant association in four studies (Fisher et al., 2008; Hall et al., 2009; Bouwman et al., 2010; Hermanns et al., 2005). In a systematic literature review of 18 studies including 2584 diabetic individuals and 1492 controls, generalized anxiety disorder (GAD) was found in 14% of patients with diabetes, and elevated symptoms of anxiety were found in 40% of patients with diabetes (Grigsby et al., 2002). Generalized anxiety disorder is found in 3–4% of the U.S. population (Grigsby et al., 2002). This literature review did not calculate the anxiety rates in the control groups as only two of the studies included these data (Grigsby et al., 2002). In a cross-sectional study of patients in a primary care clinic, depression and/or anxiety was found in 36% of patients with type 2 diabetes, versus 24% of patients with other chronic illnesses and 31% of patients without chronic illnesses (Thomas et al., 2003). One longitudinal study suggested that depression and anxiety were risk factors for type 2 diabetes, but did not examine depression and anxiety separately (Engum, 2007). Another longitudinal study suggested there were increases in anxiety severity over 18 months, but there was less persistence of anxiety symptoms compared with depressive symptoms (Fisher et al., 2008). A third study assessed anxious temperament in individuals with newly diagnosed diabetes after six months, but this study was not focused on change in anxiety symptoms over time in relation to the diagnosis (Hall et al., 2009).

There are various mechanisms by which anger and anxiety could lead to the development of type 2 diabetes. These include adverse health behaviors, such as unhealthy diet and sedentary lifestyle leading to obesity. In addition, biological abnormalities including neuroendocrine alterations in the hypothalamic-pituitary-adrenal (HPA) axis, activation of the sympathetic nervous system causing excess catecholamine release, and the release of inflammatory cytokines, all lead to insulin resistance, a diabetes risk factor (Golden, 2007).

In this study, we investigated whether 1) anger predicted incident type 2 diabetes and 2) anxiety predicted type 2 diabetes. In all of these analyses, we sought to determine if associations were independent of depressive symptoms and explained by health behaviors (i.e. physical inactivity, smoking and/or high dietary energy intake), biological factors (i.e. inflammation), and metabolic factors (i.e. waist circumference, body mass index).

RESEARCH DESIGN AND METHODS

Study population

The Multi-ethnic Study of Atherosclerosis (MESA) is a National Heart, Lung, and Blood Institute (NHLBI)-funded study initiated in July 2000, which investigates subclinical cardiovascular disease (CVD), in a population-based sample of 6,814 men and women from African-American (27.8%), Hispanic (21.9%), Chinese (11.8%), and White (38.5%) backgrounds in 6 U.S. communities: Baltimore City and Baltimore County, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; Northern Manhattan and the Bronx, New York; and St. Paul, Minnesota. Details regarding MESA's design, procedures and objectives have been published (Bild et al., 2002). Participants were assessed for type 2 diabetes at baseline, and for the development of incident diabetes during follow-up. In this study, 5,941 participants (53.6% women, mean age 61.8 years) at baseline without prevalent type 2 diabetes or cardiovascular disease were followed for a median of 9.1 years for the development of incident diabetes. The first (baseline) visit was conducted in 2000–2002. Follow-up visits 2, 3, 4, and 5 were done in 2002–2004, 2004–2005, 2005–2007, and 2010–2012, respectively. The retention rate was 92% at visit 2, 89% at visit 3, 87% at visit 4, and 76% at visit 5. Written informed consent was obtained from participants and the study was approved by Institutional Review Boards of each institution.

Assessment of Trait Anger and Trait Anxiety

Trait anger was assessed via the Spielberger Trait Anger Scale at visit 1 (Spielberger et al., 1983). Trait anger is a relatively stable and enduring personality attribute defined as the propensity to experience anger. Persons who score high in trait anger, compared to their less angry counterparts, report experiencing anger more frequently, more intensely, and with longerlasting episodes. Trait anger is scored on a scale of 10–40 and respondents rate their typical experience with anger on a 4-point scale: 1 "almost never," 2 "sometimes," 3 "often," and 4 "almost always" (Williams et al., 2000; Williams et al., 2001; Golden et al., 2006; Spielberger et al., 1983). The categories of low (10–14), moderate (15–21), and high (22–40) anger were defined by the existing categories in the literature (Williams et al., 2000; Williams et al., 2001; Golden et al., 2006).

The Spielberger Trait Anger Scale consists of two distinct subscales, trait anger temperament and trait anger reaction, which are scored in a similar manner, and scores range from 4–16 (Williams et al., 2000; Williams et al., 2001; Golden et al., 2006). The anger temperament subscale measures the degree to which a person possesses a fiery, explosive temperament. Persons who have a strong, angry temperament typically experience unprovoked (or minimally provoked) anger in a wide range of situations (Williams et al., 2001). The anger reaction subscale, on the other hand, measures the degree to which a person experiences anger in response to perceived unfair treatment, criticism, or frustration (Williams et al., 2001). Acceptable reliability and validity have been reported for the Spielberger total anger scale and the two subscales (Golden et al., 2006; Spielberger et al., 1983). In this paper, the term trait anger refers to the total trait anger score, unless otherwise specified as the anger temperament or anger reaction subscale scores.

Trait anxiety was assessed at MESA visit 1 via the Spielberger Trait Anxiety Scale (Spielberger et al., 1983). It evaluates feelings of apprehension, tension, nervousness, and worry, which increase in response to physical danger and psychological stress. Trait anxiety is reported on a scale of 10–40 and respondents rate their typical experience with anger on a 4-point scale ranging from 1 “not at all” to 4 “very much so” (Spielberger et al., 1983). The test reliability measured by alpha coefficients were high and ranged from 0.86 to 0.95 (Julian, 2011). An extensive body of research has shown that the trait anxiety scale correlates well with other validated measures of anxiety (Spielberger et al., 1983). The trait anxiety scale measures anxiety as an inherent characteristic and is less likely to detect change over time (Julian, 2011). As there were no pre-defined categories in the literature for trait anxiety, the sample was divided into quartiles based on the distribution of scores in our population.

Assessment of Diabetes Status

Type 2 diabetes was defined according to the 2003 American Diabetes Association (ADA) criteria as fasting glucose ≥7.0 mmol/L (126 mg/dL), use of oral hypoglycemic medication and/or insulin, or self-reported physician diagnosis (American Diabetes Association, 2006). Medication information was collected by transcription of medications brought into clinic. Type 2 diabetes was further subdivided into participants who were untreated (no pharmacological therapy) or treated. Incident diabetes was defined among participants who did not have prevalent diabetes at baseline but developed diabetes at subsequent visits 2 to 5.

Covariates

Covariates were assessed at baseline examination using standard protocols as previously described (Bild et al., 2002). Sex, age, race/ethnicity, years of education, and annual income were self-reported. Depressive symptoms were assessed at visit 1 using The Center for Epidemiologic Studies Depression (CES-D) Scale, a 20-item questionnaire developed to assess depressive symptoms (Radloff, 1977). Elevated depressive symptoms were defined by a CES-D score ≥16, consistent with mild-to-moderate depression or dysthymia (Beekman et al., 1997). The use of anti-depressant medications was noted.

Participants' usual diet was characterized using a 120-item food frequency questionnaire, modified from the validated Insulin Resistance Atherosclerosis Study in which comparable validity was observed for non-Hispanic white, African American, and Hispanic participants. The MESA dietary assessment was modified to include foods typically eaten by Chinese groups. The total daily caloric intake was used as a summary variable of dietary intake, and also included protein, fat, and carbohydrate intake (Mayer-Davis et al., 1999). Physical activities was assessed using the 28-item MESA Typical Week Physical Activity Survey (TWPAS) and summarized as the MET-min/week spent in total intentional exercise (Bild et al., 2002). Cigarette smoking history was self-reported as never, former, or current. Alcohol use was self-reported as never, former, or current.

Weight and height were measured using a balance beam scale and a stadiometer, respectively, with participants wearing light clothing and no shoes. Height was recorded to the nearest 0.5 cm and weight to the nearest 0.5 lb. Body-mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). All anthropometric measures were taken in duplicate and averaged.

Blood pressure and lipids were measured and categorized using standard procedures and current recommendations (Friedewald et al., 1972; Ni et al., 2006; Chobanian et al., 2003; Pickering et al., 2005). Hypertension was defined by JNC VI (1997) criteria hypertension of systolic blood pressure >=140 mmHg or diastolic blood pressure >=90 mmHg. The lipid categories were determined by NCEP 2001 guidelines, and included total cholesterol, LDL, HDL, and triglycerides. For total cholesterol, desirable was < 200 mg/dL. For LDL, optimal was < 100 mg/dL. For HDL, low was < 40 mg/dL and high was ≥ 60 mg/dL. For triglycerides, normal was < 150 mg/dL. Interleukin (IL-6) and high sensitivity C-reactive protein (CRP) were measured using standard techniques that were previously described. Microalbuminuria was assessed using a spot urine sample with standard laboratory techniques previously described (Bild et al., 2002).

Statistical Analysis

Bivariate analyses—Differences in continuous and categorical variables between those who developed incident diabetes and those who did not were compared using Student's t-test and Chi-square tests, respectively. Non-normally distributed continuous variables were compared using the Wilcoxon Rank Sum test.

Multivariable analyses

Anger as a predictor of diabetes: Trait anger was examined as a continuous variable. Trait anger was also divided by total score into categories of low (10–14), moderate (15–21), and high (22–40) anger (Williams et al., 2000; Williams et al., 2001). The relative hazard of incident type 2 diabetes at visits 2, 3, 4, and 5 was calculated for those with moderate and high trait anger compared to those with low trait anger using Cox proportional hazards model. Secondary analyses were performed examining the trait anger reaction and temperament subscales as predictors of diabetes. In these analyses, the relative hazard of diabetes was calculated for each 1-unit increment in anger reaction and anger temperament subscale score.

To evaluate potential explanatory factors, a series of multivariable models were created. The base model included adjustment for age, sex, race/ethnicity, MESA site, and education. Model 2 included the base model plus adjustment for depressive symptoms (modeled as continuous CES-D score) and anti-depressant medications. The subsequent models were created with groups of related covariates to help determine which sets of covariates might explain the observed associations. Subsequent models included all variables in Model 2 plus the following additional adjustments: Model 3 (lifestyle—physical activity, dietary intake, smoking status, alcohol use), Model 4 (inflammatory—IL-6, CRP), and Model 5 (metabolic—waist circumference, blood pressure, lipids). Within the metabolic factors, waist circumference and BMI were assessed for correlation. Interaction between sex and race/ethnicity was assessed in anger models. Because there was not significant effect modification by sex or race/ethnicity, analyses were conducted unstratified.

Anxiety and Diabetes: Trait anxiety was also divided into quartiles based on the distribution of the sample since there were no pre-defined categories in the literature. This sample showed that most individuals had low anxiety, with a median anxiety score of 15 on a scale of 10–40. The relative hazard of incident diabetes at visits 2, 3, 4, and 5 was calculated for those in the highest quartiles of trait anxiety compared to those in the lowest quartile using Cox proportional hazards model. Trait anxiety was also examined as a continuous variable. In secondary analyses, the relative hazard of diabetes was calculated for each 1-unit increment in trait anxiety score. We used the same multivariable adjustments as outlined above for trait anger. Of note, diabetes was not tested as a predictor for change in trait anxiety score since trait anxiety would not be expected to change acutely and reflects an individual's chronic psychological temperament.

There was no evidence to contradict the proportionality assumption based on Schoenfeld residuals after fitting unadjusted and adjusted models. SAS v9.2 and Stata v12 were used for all analyses.

RESULTS

For this study, participants with type 1 diabetes (n=10) or missing data on diabetes at baseline (n=24) were excluded from the total MESA sample of 6,814 participants. For Cox models of incident diabetes, further exclusions were participants with prevalent type 2 diabetes at baseline (n=849) or no follow-up visits (n=333). There were 5,598 participants (82% of the cohort) eligible for survival analyses. After the exclusion of participants with missing data, there were 5,571 participants with data on trait anger and 5,566 participants with data on trait anxiety at baseline.

Baseline characteristics

Table 1 summarizes the baseline characteristics according to diabetes incidence. Of 5,598 participants who did not have diabetes at baseline, there were 41,981 person years of follow-up. There were 695 incident type 2 diabetes cases over a total period of 11.4 years until visit 5 concluded, resulting in a incidence rate of 1.7 cases per 100 person years. Compared to individuals who did not develop diabetes, those who developed diabetes were younger, less likely to be white, less educated, consumed more daily calories, including more protein and

fat intake, exercised less, were less likely to drink alcohol, and had higher blood pressure, waist circumference, BMI, fasting glucose, triglycerides, and microalbuminuria. Individuals who developed diabetes also had lower HDL cholesterol than those who did not develop diabetes. The two groups did not differ in sex, smoking status, depressive symptoms, or anti-depressant medication use.

Univariate and Multivariable Analyses

Anger and Incident Diabetes—In Supplemental Table 1, the characteristics of participants in low, moderate, and high trait anger categories were compared. Compared to those with low and moderate levels of trait anger, participants with high trait anger were younger, more likely to be Hispanic, less educated, consumed more daily calories, including more protein, fat, and carbohydrate intake, exercised less, were more likely to smoke, had larger waist circumference, and higher levels of depressive symptoms and antidepressant medication use. Participants with low trait anger were more likely to be black, less likely to drink alcohol, and had higher blood pressure and IL-6. There were no significant group differences for sex, BMI, fasting glucose, lipids, CRP and microalbuminuria.

In table 2, the relative hazards of developing type 2 diabetes by trait anger category are shown. In the analysis of trait anger as a continuous variable, the trend suggested an association of borderline statistical significance (OR=1.02, 95% CI 1.0–1.04, p=0.06) (results not shown). Of the 244 participants with baseline high trait anger, 42 (17.2%) developed type 2 diabetes over follow-up. In our base model, individuals in the high trait anger category had a significantly higher risk of developing incident type 2 diabetes (HR 1.50; 95% CI 1.08–2.07) relative to the low anger group (Table 2). The association remained significant with the adjustment for depressive symptoms, lifestyle factors, inflammatory markers, and the metabolic factors of blood pressure and lipids. However, the association was attenuated and became non-significant following adjustment for the specific metabolic factor of waist circumference (HR=1.32; 95% CI 0.94–1.86) (Table 2). When adjusting for BMI instead of waist circumference, similar results were found. Waist circumference and BMI were highly correlated with a correlation coefficient of 0.84.

There was a significant association between anger reaction and incident type 2 diabetes (Table 3). The association remained significant after multivariable adjustment (HR=1.07; 95% CI 1.03–1.11) (Table 3). There was no association of anger temperament with incident type 2 diabetes.

Anxiety and Incident Diabetes—In the analysis of trait anxiety as a continuous variable and divided into quartiles, there was no significant association with incident diabetes in any of our multivariable models (Supplemental Table 2).

CONCLUSIONS

Individuals with high trait anger at baseline had a 50% increased risk of developing type 2 diabetes in follow-up visits 2 to 5, compared with those in the low anger category; moderate anger did not differ from low anger in predicting incident diabetes. The association of high anger and incident diabetes was attenuated following adjustment for metabolic factors,

specifically waist circumference or BMI. There was also an increased risk of diabetes for individuals with high anger reaction, which persisted following multivariable adjustment. No significant associations were found with trait anxiety and incident type 2 diabetes.

Our findings regarding the characteristics of individuals with high trait anger were similar to those of the Atherosclerosis Risk in Communities (ARIC) study by Williams, et al. (2000) examining anger proneness and coronary heart disease risk. In both ARIC and MESA, individuals with high trait anger were likely to be younger, less educated, more likely to smoke, and had increased adiposity. Our findings differed from those of the Atherosclerosis Risk in Communities (ARIC) study by Golden, et al. (2006) examining anger and incident type 2 diabetes. In MESA, but not in ARIC, high total trait anger was associated with an increased risk of type 2 diabetes. Also, in contrast to the ARIC study, which showed an association of higher anger temperament with type 2 diabetes risk (Golden et al., 2006), our study showed an association of higher anger reaction but not higher anger temperament with type 2 diabetes risk. In both the ARIC and MESA studies, adjustment for measures of adiposity (e.g. BMI), attenuated the association of anger temperament and overall trait anger, respectively, with incident type 2 diabetes (Golden et al., 2006).

The potential mechanisms by which high anger could lead to diabetes include the effects of anger on adverse health behaviors such as poor diet and sedentary lifestyle. Previous studies have shown associations between hostility and increased caloric consumption (Scherwitz et al., 1992). These lifestyle changes may lead to increased BMI and visceral adiposity, with increased insulin resistance (Golden, 2007). In addition, obese individuals have been found to be more vulnerable to emotional eating as a means of coping with anger (Appelhans et al., 2011). Anger and hostility have been associated with visceral adiposity in studies using indirect measurement with waist to hip ratio (Wing et al., 1991) and direct measurement with computed tomography (CT) (Raikkonen et al., 1999). Our data support this hypothesis, as individuals with high trait anger consumed more daily calories, exercised less, and had larger waist circumference compared with those with lower trait anger score. For this study, the dietary data collected did not include caffeine intake, so this variable could not be investigated. It is possible that high trait anger might activate neuroendocrine (e.g. HPA axis, sympathetic nervous system) and inflammatory pathways associated with insulin resistance (Golden, 2007). In our cohort, IL-6 and CRP levels were similar in those with high and low trait anger, and associations persisted following adjustment for these factors. We did not have measures of neuroendocrine function and thus we were unable to assess this as a potential contributor to our associations.

High anger reaction may be more closely linked to higher impulsivity, which has been associated with binge eating episodes (Engel et al., 2007). The literature suggests that poor self-control and aggressive behavior are also associated with impaired cerebral glucose utilization (DeWall et al., 2011). In addition, high anger reaction may also underlie the propensity to acutely activate physiological systems, which increase insulin resistance and the risk of diabetes. These acute changes may have effects that extend beyond the momentary experience of anger. In contrast, anger temperament may not have the same enduring effects on neuroendocrine and inflammatory pathways. Our data did not show anger temperament as a risk factor for type 2 diabetes, but this may be due to an adaptive

mechanism of biological systems to anger temperament, a particular danger of high anger reaction, or a limitation of the available anger subscales. Further research is needed to understand the long-term effects of anger on metabolic and biological factors. Our data showed that the significant association between anger reaction and incident type 2 diabetes persisted after adjustment for demographic factors, depressive symptoms, as well as lifestyle, inflammatory, and metabolic factors. Participants with a prior history of type 2 diabetes did not show an increase in anger or a greater risk of developing high trait anger. Trait anger may be inherent to the disposition of the individual, and as such may be less likely to change over time.

We did not find a significant association between trait anxiety and incident type 2 diabetes. Prior studies examining the association of anxiety with diabetes have showed mixed results. The previous longitudinal studies noted overlap in anxiety and depressive symptoms, which may have affected the results (Engum, 2007; Fisher et al., 2008), since depressive symptoms are known predictor of type 2 diabetes (Golden et al., 2008). Our findings were unchanged after adjusting for depressive symptoms or anti-depressant use. These data suggest that behavioral and biological pathways linking depressive symptoms and diabetes are likely not implicated in anxiety and that anxiety may not be an important psychological factor in predicting risk of future diabetes.

Our study has several strengths. First, it is one of the few studies exploring trait anxiety as a risk factor for incident type 2 diabetes. Second, we assessed trait anger and anxiety using standardized, validated questionnaires. Third, we had a long duration of longitudinal follow-up (11.4 years) in a multi-ethnic cohort. Finally, MESA collected detailed information regarding covariates and potential confounders that were adjusted for in our analyses.

Several limitations should be kept in mind in interpreting our data. First, we did not have direct measurement of hormonal or sympathetic nervous system function, which are additional potential mediators of the trait anger-diabetes association. Second, these analyses reflect the importance of waist circumference and BMI in the anger-diabetes association; however, we did not have direct measurement of visceral adiposity or body composition. Third, the anger reaction and anger temperament scales are based on a limited number of items, which may not fully capture the dimensions of anger. For future studies, the Novaco Anger Scale and Provocation Inventory (NAS-PI), may be considered as a more detailed anger assessment (Mills et al., 1998). The NAS-PI is a self-report questionnaire with 85 items that measure the experience of anger and the subscales include the cognitive, emotional, behavioral, and self-regulation dimensions of anger (Mills et al., 1998). Fourth, after accounting for the most common and well-studied risk factors, there may be still other factors which has not been accounted for explaining the association between trait anger and type 2 diabetes.” Finally, our analyses of trait anxiety were based on quartiles of the distribution sample rather than predefined categories as were available for trait anger. We only included trait anxiety at baseline so we were unable to determine if change in anxiety status might be a better predictor of diabetes risk.

We have identified high trait anger and anger reaction as risk factors for type 2 diabetes. This suggests that psychological interventions to address anger management should also

incorporate recommendations for avoiding unhealthy lifestyle responses to anger that might promote future metabolic risk. Further studies are needed to explore the mechanisms of the anger-diabetes relationship and to assess the effect of behavioral interventions for anger management and their effects on risk modification and disease prevention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

We examined the association of trait anger and trait anxiety with incident T2DM.

High total trait anger was associated with incident T2DM relative to low total trait anger.

Higher anger reaction was also associated with incident T2DM.

Table 1

Selected Baseline Characteristics by Incident Diabetes Status

	Incident Diabetes n=695	**No Incident Diabetes n=4903**	**p-value**
	% or Mean ± SD	**% or Mean ± SD**	
Age (years)	60.8 ± 9.5	61.7 ± 10.3	0.029
Female (%)	51.9	53.4	0.47
Race ethnicity (%)			<0.001
White	30.2	43.8	
Chinese	11.8	11.5	
Black	31.1	25.0	
Hispanic	26.9	19.7	
Education Status (%)			0.002
Less than high school	19.45	15.0	
High school	19.45	17.6	
College or greater	61.1	67.4	
Current Cigarette Smoking (%)	12.1	12.9	0.56
Current Alcohol Use (%)	54.0	58.9	0.014
Daily Caloric Intake (calories/day) §	1586 (1155, 2153)	1491 (1111, 2040)	0.016
Protein Intake (g/day) §	62 (44, 85)	60 (42, 81)	0.04
Fat Intake (g/day) §	61 (41, 87)	55 (39, 79)	<0.001
Carbohydrate Intake (g/day) §	194 (142, 262)	187 (138, 254)	0.11
Intentional Exercise (met-min/wk) §	660 (0, 1838)	900 (210, 2100)	0.003
Hypertension (%)	53.0	39.4	<0.001
Systolic blood pressure (mmHg)	130 ± 21	125 ± 21	<0.001
Waist circumference (cm)	105 ± 14.1	96 ± 13.6	<0.001
Body-mass index (Kg/m^2)	31.1 ± 5.8	27.6 ± 5.1	<0.001
Fasting glucose (mg/dl)	101 ± 13	88 ± 9	<0.001
Total cholesterol (mg/dl)	194 ± 36	195 ± 35	0.60
LDL-cholesterol (mg/dl)	117 ± 32	118 ± 31	0.66
HDL-cholesterol (mg/dl)	46.7 ± 12.2	52.4 ± 15.2	<0.001
Triglycerides (mg/dl) §	133 (93, 188)	106 (74, 152)	<0.001
IL-6 (pg/mL) §	1.38 (0.91, 2.15)	1.12 (0.72, 1.74)	<0.001
C-reactive protein (mg/L) §	2.64 (1.24, 6.02)	1.69 (0.76, 3.91)	<0.001
Micro/macro albuminuria (%)	10.4	5.9	<0.001
CES-D ≥ 16 (%)	12.8	11.9	0.50
Antidepressant Use (%)	9.9	9.5	0.70
Spielberger Trait Anger Categories Low (10–14) Medium (15–21) High (22–40)	 55.2 40.7 4.1	 50.8 43.1 6.1	 0.008

	Incident Diabetes n=695	**No Incident Diabetes n=4903**	**p-value**
	% or Mean ± SD	**% or Mean ± SD**	
Spielberger Trait Anxiety Quartiles (Q)			
Q1 (10–12)	25.4	25.8	
Q2 (13–15)	26.4	26.8	
Q3 (16–19)	26.0	27.4	
Q4 (20–40	25.4	20.0	0.44

χ-square tests were used to compare categorical covariates, and *F*-tests (linear models) and Wilcoxon Rank Sum tests were used to compare means and medians of continuous covariates, respectively

Table 2

Relative hazards of developing Type 2 Diabetes by Trait Anger Category

Trait Anger Category	Model 1: (Base)	Model 2: (Depression)	Model 3: (Lifestyle)	Model 4: (Inflammatory)	Model 5: (Metabolic)	Model 6: (Fully Adjusted)
Low (10–14) n=3044	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Moderate (15–21) n=2283	1.13 (0.97, 1.33)	1.13 (0.96, 1.33)	1.20 (1.01, 1.42)	1.14 (0.96, 1.34)	1.13 (0.96, 1.33)	1.24 (1.04, 1.47)
High (22–40) n=244	1.50 (1.08, 2.07)	1.47 (1.05, 2.05)	1.48 (1.04, 2.12)	1.45 (1.04, 2.03)	1.32 (0.94, 1.86)	1.45 (1.00, 2.09)

Model 1 (Base): Adjusted for age, sex, race/ethnicity, education and MESA site
Model 2 (Depression): Model 1 + depressive symptoms (as continuous CES-D score) + antidepressants
Model 3 (Lifestyle): Model 2 + exercise, diet, smoking, alcohol use
Model 4 (Inflammatory): Model 2 + interleukin 6 (IL-6), C-reactive protein (CRP)
Model 5 (Metabolic): Model 2 + waist circumference, blood pressure (BP), lipids
Model 6 (Fully Adjusted): Base + depressive symptoms + antidepressants + lifestyle (exercise, diet, smoking, alcohol use) + inflammatory (IL-6, CRP) + metabolic (waist circumference, BP, lipids)

Table 3

Relative hazards of developing Type 2 Diabetes by Trait Anger Subscale

Anger Subscale	Model 1: (Base)	Model 2: (Depression)	Model 3: (Lifestyle)	Model 4: (Inflammatory)	Model 5: (Metabolic)	Model 6: (Fully Adjusted)
Temperament § (4–16)	1.02 (0.97, 1.06)	1.01 (0.97, 1.06)	1.01 (0.97, 1.06)	1.02 (0.97, 1.06)	1.00 (0.95, 1.05)	1.01 (0.97, 1.07)
Reaction § (4–16)	1.06 (1.02, 1.10)	1.06 (1.02, 1.10)	1.07 (1.03, 1.11)	1.07 (1.03, 1.11)	1.05 (1.02, 1.09)	1.07 (1.03, 1.11)

§Per 1-unit increase in scale, range from 4–16

Model 1 (Base): Adjusted for age, sex, race/ethnicity, education and MESA site
Model 2 (Depression): Model 1 + depressive symptoms (as continuous CES-D score) + antidepressants
Model 3 (Lifestyle): Model 2 + exercise, diet, smoking, alcohol use
Model 4 (Inflammatory): Model 2 + interleukin 6 (IL-6), C-reactive protein (CRP)
Model 5 (Metabolic): Model 2 + waist circumference, blood pressure (BP), lipids
Model 6 (Fully Adjusted): Base + depressive symptoms + antidepressants + lifestyle (exercise, diet, smoking, alcohol use) + inflammatory (IL-6, CRP) + metabolic (waist circumference, BP, lipids)

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