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Research paper

The association between insulin resistance and depression in the Korean general population

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ABSTRACT

Background: Previous studies showed that the insulin resistance (IR) could be related to depression. However, this association is still equivocal in the general population. Herein, we aimed to investigate the association between IR and depressive symptoms in a large sample in South Korea.

Methods: A cross-sectional study was carried out for 165,443 Korean men and women who received a health checkup including various clinical parameters and the Center for Epidemiologic Studies Depression scales (CES-D). Subjects were stratified into subgroups by CES-D score, sex, age, and presence of diabetes. The odd ratios (ORs) for homeostasis model assessment of insulin resistance (HOMA-IR) were compared between groups using multivariable logistic regression analyses.

Results: After adjusting covariates (e.g. smoking, family income, marriage state, unemployment status, average alcohol use, BMI, physical activity, systolic blood pressure, diabetes), increased IR was weakly associated with greater depressive symptoms (adjusted OR=1.01 [95% CI 1.0001–1.03]). Subgroup analysis revealed this association was statistically significant in females (adjusted OR=1.03, [95% CI 1.001–1.06]), non-diabetic group (adjusted OR=1.04, [95% CI 1.02–1.06]), and young participants under the age of thirty (adjusted OR=1.17, [95% CI 1.07–1.27]). But we couldn't find significant association in diabetic and middle to elderly participants.

Conclusions: This study demonstrates that there is a relationship between IR and depressive symptoms in the Korean general population. Results from this epidemiological study revealed that young adults and non-diabetic individuals with increased IR may be related with depressive symptoms.

1. Introduction

During the past several decades, the prevalence of type 2 diabetes mellitus (T2DM) and metabolic syndrome has been increasing globally (Shaw et al., 2010; Grundy, 2008). T2DM is now a major cause of morbidity and mortality in both developed and developing countries. The etiology of metabolic disorders is complex and multifactorial, but increasing prevalence of obesity, physical inactivity, sedentary lifestyle or an aging population are regarded as major contributors. Recently, the role of psychiatric disorders on metabolic parameters, including major depressive disorder (MDD), is increasingly being recognized (Anderson et al., 2001; Mezuk et al., 2008; Eaton et al., 1996; Schmitz et al., 2016).

The underlying etiology and the pathophysiological link between

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depressive symptom and metabolic disorder such as T2DM have yet to be elucidated; however, there were several possible explanations. Behavioral risk factors such as psychological stress and circadian dysfunction may predispose T2DM and depression (Singh et al., 2015, 2012). Recent meta-analysis showed a relationship between depression and diet quality (van Dooren et al., 2013; Rotella and Mannucci, 2013; Valkanova and Ebmeier, 2013), and diet pattern is closely related with metabolic disorder. Stress hormones including cortisol and catecholamine which are increased by depression can be another underlying pathophysiology because it can trigger inflammation in the blood vessel, cardiomyocytes, and neuron (Aschbacher et al., 2014). Furthermore, it has been hypothesized that insulin resistance (IR) also play a key role in its pathophysiology (Chen et al., 2016; Wahlqvist et al., 2012). IR is commonly associated with T2DM and the metabolic syndrome (Martin et al., 1992; Grundy, 1999).

1.1. Objectives and hypothesis

Although several previous studies have investigated the association between depression and IR (Pearson et al., 2010; Lustman et al., 2000; Khambaty et al., 2014; Lawlor et al., 2003; Adriaanse et al., 2006; Pan et al., 2008); however, there is a paucity of data evaluating this association at the population level, particularly in Asia. If individuals with depression have a high risk of diabetes or metabolic syndrome, they are more likely to have increased IR even in normal and pre-diabetes condition. Therefore, we conducted a large scale (> 160,000 participants) study to investigate the relationship between IR and depressive symptoms in the Korean general population.

2. Methods

2.1. Ethical aspects

Ethics approvals for the study protocol and analysis of the data were obtained from the institutional review board of Kangbuk Samsung Hospital. The informed consent requirement was waived by the Institutional Review Board because the researchers only retrospectively accessed a de-identified database for analytical purposes.

2.2. Study design and participants

A cross sectional study was conducted to assess the relationship between depression and IR. Data were obtained from the Kangbuk Samsung Health Study (KSHS) cohort. The majority of study participants were Korean men and women undergoing a medical health check-up program at the Health Promotion Center of Kangbuk Samsung Hospital, Sungkyunkwan University. According to the Korea's Industrial Safety and Health law, all employees are required to participate in either annual or biennial health check-up, and participants and their companies freely choose any certified healthcare center in South Korea. Therefore, the study participants came from all regions in South Korea, but most of our study participants were residents in Seoul metropolitan area (> 20 million population) because the locations of the Health Promotion Center of Kangbuk Samsung Hospital are in Seoul and Suwon. Family members of Korean employees also participated in this regular health check-up program.

Between January 2014 to December 2014, a total 175,970 men and women 18–91 years old) had received regular health check-ups at the Health Promotion Center of Kangbuk Samsung Hospital and participated the present study.

2.3. Clinical and laboratory measures

Study data included a medical history, a physical examination, information provided by a questionnaire, anthropometric measurements and laboratory measurements. All study participants were asked to respond to a health-related behavior questionnaire, which included the topics of alcohol consumption, smoking and exercise. The questions about alcohol intake included the frequency of alcohol consumption on a weekly basis and the typical amount that was consumed on a daily basis. The type of alcoholic beverage also was asked. Next, we calculated the average amount of alcohol intake per day. Smoking history was assessed by self-reported questionnaire and categorized as never, former and current smoker. The amount and duration of smoking also were asked in this questionnaire. The degree of physical activity was evaluated by the Korean-validated version of the International Physical Activity Questionnaire Short Form (IPAQ-SF), and Oh et al. (2007) showed the reliability and validity of the Korean version of IPAQ-SF. Physical activity of participants was classified three categories: inactive, minimally active, and health-enhancing physically active (HEPA) (Craig et al., 2003). All participants were also asked to respond to questions about family income per month, marriage state, and employment status. Presence of diabetes mellitus was defined as fasting serum glucose level (i.e., ≥126 mg/dL), serum hemoglobin A1c (Hb A1c) level (i.e., ≥6.5%), the current use of any blood glucose-lowering medications, or prior history of diabetes. Body mass index (BMI) was calculated by dividing weight (kilograms) by height squared (meters2). Hypertension was defined as either the current use of antihypertensive medication, past history of hypertension or as having a measured blood pressure (BP) ≥140/90 mmHg at initial examinations. Trained nurses obtained sitting BP levels using automatic BP equipment (53000-E2, Welch Allyn, USA) after a 5 min rest.

Blood samples were collected after more than 12 h of fasting and were drawn from an antecubital vein. Insulin levels were measured with immunoradiometric assays (Biosource, Nivelles, Belgium). IR was calculated by homeostasis model assessment-insulin resistance (HOMA-IR) and obtained using the following formula: HOMA-IR=fasting serum insulin (uU/mL)×fasting serum glucose (mg/dl)/405.

The fasting serum glucose was measured using the hexokinase method. HbA1c was measured using an immunoturbidimetric assay with a Cobra Integra 800 automatic analyzer (Roche Diagnostics, Basel, Switzerland). Total cholesterol and triglyceride were measured using enzymatic colorimetric tests (Advia 1650 Autoanalyzer; Bayer Diagnostics; Leverkusen, Germany). High sensitivity C-reactive protein (hsCRP) was analyzed by particle-enhanced immunonephelometry with the BNII System (Dade Behring, Marburg, Germany). Serum creatinine was measured using the alkaline picrate (Jaffe) method. The clinical laboratory has been accredited and participated annually in inspections and surveys by the Korean Association of Quality Assurance for Clinical Laboratories.

2.4. Measure of depression

The severity of depression was evaluated by the Korean versions of the Center for Epidemiologic Studies Depression Scale (CES-D) (Cho and Kim, 1998). The CES-D is a self-report questionnaire designed to assess the current prevalence of depressive symptom in the general population (Radloff, 1977). It is a 20-item questionnaire with a four points scale. The Korean version of the CES-D demonstrates high reliability (Cronbach α=0.893) and test-retest reliability (Pearson r coefficient, 0.68; $P < 0.001$) (Cho and Kim, 1998). Depression was defined as a CES-D score of more than 16. At the same time, to assess severity of IR according to CES-D scale cut off points, participants' CES-D score was categorized as follows: mild depression (score: 16–20), moderate depression (score: 21–24), and severe depression (score: ≥25).

2.5. Statistical analysis

Data are presented as means ± standard deviation for continuous variables and as percentages for categorical variables. All study