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Association of insulin resistance with depression: cross sectional findings from the British women’s heart and health study
Debbie A Lawlor, George Davey Smith, Shah Ebrahim

A large cohort study of nearly 15,000 individuals found that indicators of insulin sensitivity were associated with increased risk of suicide.1 The authors assumed that insulin resistance was the key factor responsible. Insulin resistance is a determinant of free fatty acids in the blood, which are in turn important in tryptophan metabolism and brain serotonin concentrations.2 3 Individuals who are insulin resistant may therefore have higher serotonin concentrations and as a result be less likely to be depressed.4 We know of no previous study that has assessed the association between insulin resistance and depression in humans.

Participants, methods and results
We assessed this association in a cross sectional analysis of 4286 women aged 60-79 who were randomly selected from general practitioners’ lists in 23 British towns.5 We used the homoeostasis model assessment method (HOMA score), derived from fasting insulin and glucose concentrations to assess insulin resistance.6 We used three indicators of depression: current use of antidepressant medication, self report of ever having received a diagnosis of depression from a doctor, and the EQ5D mood question of the EuroQOL.5 Participants brought all of their medications to an interview with a nurse. We used the British National Formulary (www.bnf.org/) to code medications; “antidepressants” included any medication in section 4.3. Participants whose response to the EQ5D mood question was that they were “today feeling either moderately or extremely anxious and/or depressed” were coded as currently anxious or depressed.

We categorised women without diabetes into quarters of HOMA score and added a fifth category of women with diabetes. We estimated proportions of women with depression for each of these HOMA score and diabetes categories. We used multiple logistic regression to assess the effect of insulin resistance on depression, with adjustment for potential confounding factors. In all analyses we used robust standard errors, allowing for potential clustering between women from the same town, to calculate confidence intervals and P values.

The prevalence of depression decreased linearly with increasing insulin resistance among women without diabetes and then increased among women with diabetes (figure). The age adjusted odds ratio (95% confidence interval) of current antidepressant use per increase in one category (quarters of the distribution) of HOMA score among non-diabetic women was 0.84 (0.74 to 0.97, P = 0.01). Similar results for ever being diagnosed with depression and reporting feeling anxious or depressed were 0.84 (0.74 to 0.97, P = 0.006) and 0.89 (0.79 to 0.99, P = 0.04). None of these associations was altered by further adjustment for waist:hip ratio, body mass index, smoking, alcohol consumption, physical activity, and social class during adulthood and childhood.

Comment
Insulin resistance is inversely associated with depression. Our results are consistent with a large prospective study that has assessed the association between insulin resistance and depression in humans.

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(a) Prevalence % (95% confidence interval) of use of antidepressant medication against quarters of HOMA score (insulin resistance) and diabetes among British women aged 60-79. (b) Prevalence % (95% confidence interval) of a self report of ever being diagnosed by a doctor with depression against quarters of HOMA score (insulin resistance) and diabetes among British women aged 60-79. (c) Prevalence % (95% confidence interval) of a self report of feeling depressed or anxious against quarters of HOMA score (insulin resistance) and diabetes among British women aged 60-79.
Drug points

Pulmonary embolism possibly associated with olanzapine treatment

Inger Marie Waage, Ane Gedde-Dahl

Antipsychotic drugs have been associated with an increased risk of venous thromboembolism. We report for the first time the case of a patient who developed a pulmonary embolism after starting treatment with olanzapine.

A 28 year old man was admitted to hospital due to a psychotic disorder. Treatment with olanzapine (10 mg/day) was started, and the dose was gradually increased to 30 mg/day. He also received levomepromazine (50 mg/day), oxacipram (10 mg/day), and fluoxetine (1 mg/day). After 10 weeks, the patient complained of respiratory dyspnoea, no tachypnoea, no fever, and normal blood pressure. Clinical examination showed no auscultatory findings, no dyspnoea, no tachypnoea, no fever, and normal blood pressure and heart rate. Blood analysis showed raised concentrations of C reactive protein (113 mg/l (normal range < 10 mg/l)), fibrinogen (6 g/l (2-4 g/l)), and D-dimer (0.89 mg/l (< 0.50 mg/l)). Spiral computed tomography showed a pulmonary embolism in the left lower lobe. Standard anticoagulant treatment was started, and the patient recovered. Olanzapine was discontinued, and his medication change to quetiapine.

Recent reports suggest an association between clozapine and venous thromboembolic events. However, thromboembolic complications have not previously been described in patients taking olanzapine. The sedating effects as well as the weight gain associated with this antipsychotic treatment can lead to a more sedentary lifestyle, thus creating predisposing conditions for venous thrombosis. In this case, the patient was overweight (body mass index 28.5), but his weight had not substantially changed since starting to take olanzapine. He was otherwise healthy, and his level of physical activity was normal. Tests for possible coagulation disorders—including tests for antiphospholipid antibodies (immunoglobulin lupus anticoagulants and anticardiolipin antibodies), mutation of the methyleneetetrahydrofolate reductase C677T thermolabile variant, prothrombin G20210A mutation, activated protein C resistance, protein C, protein S, antithrombin III, and homocysteine—did not show any underlying risk factors. This leaves the question of the medication’s possible direct causal effect.

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