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Insulin resistance and depressive symptoms in middle aged men: findings from the Caerphilly prospective cohort study

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Insulin resistance may protect against depression, possibly through an effect on circulating free fatty acid concentrations and brain serotonin concentration, although a recent study contradicted these findings. Studies to date have either used indirect measures of insulin resistance, or they have been cross sectional. We assessed the association of insulin resistance with depressive symptoms in a prospective cohort.

Participants, methods, and results

The Caerphilly cohort study has been described in detail before. In phase I (1979-83), 2512 (89% of eligible) men aged 45-59 years from Caerphilly in Wales provided fasting blood samples. Insulin resistance (homeostasis model assessment (HOMA) score) was derived from fasting insulin and glucose. HOMA scores were not calculated for men with diabetes or high fasting glucose (>7.0 mmol/l).

In phases II (1984-88), III (1988-93), and IV (1993-97), depressive symptoms were measured by the 30 item depression inventory. There was no association between any HOMA scores, fasting insulin, or diabetes and GHQ score. We also found no associations between body mass index, systolic blood pressure, high density lipoprotein cholesterol, or (logged) triglyceride concentration and GHQ in either prospective or cross sectional analyses (all P values >0.3).

Comment

Insulin resistance was not associated with reduced depressive symptoms in a prospective study of middle aged men. This contradicts our earlier findings in a cross sectional study of older women, in which there was an inverse association with both clinically diagnosed depression and use of antidepressant drugs, and the findings of a second cross sectional study which found a positive association between insulin resistance and depression assessed using the Beck's depression inventory. These contradictory findings may be due to the cross sectional nature of the earlier studies. A large prospective study, in which reverse causality would be unlikely, found that indicators of insulin sensitivity were associated with suicide risk. Taken together these findings indicate that insulin resistance may protect against only severe depression.

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Insulin resistance and diabetes at baseline (1979-83) and GHQ score (indicative of depressive symptoms) at different phases of follow-up in middle aged men in the Caerphilly prospective cohort study

<table>
<thead>
<tr>
<th>Phase of follow up</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>Phase of follow up</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td>No with GHQ data</td>
<td>1619</td>
<td>1236</td>
<td>1088</td>
<td>No with high HOMA</td>
<td>362</td>
</tr>
<tr>
<td>No with high GHQ</td>
<td>289</td>
<td>271</td>
<td>63</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Age and time of blood sampling adjusted prevalence of high GHQ score by insulin resistance or diabetes (% (95% CI)):
- Lowest fourth HOMA: 22.9 (19.1 to 27.2), 21.7 (17.4 to 26.7), 24.1 (19.5 to 29.4), 7.9 (5.1 to 12.8)
- 2nd fourth HOMA: 21.4 (17.7 to 25.7), 22.2 (18.0 to 27.2), 21.6 (17.0 to 27.0), 4.3 (2.4 to 7.6)
- 3rd fourth HOMA: 24.6 (20.4 to 29.1), 23.7 (19.2 to 28.9), 27.0 (21.9 to 32.7), 6.7 (4.1 to 10.7)
- Highest fourth HOMA: 20.5 (16.7 to 25.0), 26.8 (22.1 to 32.4), 28.8 (23.4 to 34.9), 7.3 (4.4 to 11.9)
- Diabetes or high fasting glucose: 19.5 (11.1 to 31.9), 16.3 (7.5 to 31.8), 12.3 (4.7 to 28.5), 4.0 (0.6 to 2.3)

Our assessment of depression was based on GHQ rather than clinical assessment, and if insulin resistance is only protective against severe depression then this measure may be inadequate to detect an association. Also, any measurement error in our assessment of depression would tend to dilute the results. We validated the score, however, against a clinical interview in a subgroup.

The contradictory results concerning the association of insulin resistance with depression and suicide warrant further research. Future studies might include trials of the effects on insulin resistance of treating depression. Observational studies should ideally use standardised diagnostic criteria for depression and prospectively assess the association of insulin resistance with differing severities.

The Caerphilly study was done by the former Medical Research Council Epidemiology Unit (South Wales) and was funded by the Medical Research Council of the United Kingdom. The department of social medicine, University of Bristol, is custodian for the Caerphilly database. We thank the men who participated in the study.

Contributors: YB-S, GDS, SE, and DAL developed the study idea. SAS validated the GHQ data. JV initiated the Caerphilly study, and YB-S, JEJG, and JWGY are responsible for the continued management of the study. DAL did the analysis and wrote the first draft of the paper, and all authors contributed to the final version. DAL and YB-S are guarantors.

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Competing interests: None declared.

Ethical approval: Phases I-III of the Caerphilly study were approved by Cardiff Local Research Ethics Committee and later phases by Gwent Research Ethics Committee.

What is already known on this topic
Cross sectional studies and those using indirect measurements indicate that insulin resistance may protect against depression.

What this study adds
Insulin resistance was not associated with reduced depressive symptoms in a prospective study of middle aged men.


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