Impaired Glucose Homeostasis in First-Episode Schizophrenia

Brian Miller, MD, PhD, MPH
Schizophrenia and Type 2 Diabetes

- Schizophrenia is associated with a significantly increased prevalence of type 2 diabetes\(^1\)

- Although antipsychotic use may contribute, associations between schizophrenia and diabetes were observed in the pre-antipsychotic era

- A meta-analysis did not find an increased prevalence of type 2 diabetes in first-episode psychosis (FEP)\(^2\); however . . .
Schizophrenia and Type 2 Diabetes (2)

- Even in the absence of frank diabetes, this does not preclude abnormalities in glucose metabolism that may predate diabetes in patients with FEP.

- There is evidence for other metabolic abnormalities in patients with FEP, including inflammation and oxidative stress. These findings suggest associations between schizophrenia and metabolic dysfunction that may be independent of the effects of antipsychotics, but which are further exacerbated by psychotropic medications and other risk factors.
Pillinger and colleagues\textsuperscript{6} conducted a meta-analysis of glucose homeostasis in patients with FEP and controls.

They hypothesized that there would be evidence of alterations in glucose homeostasis in patients with FEP.
Study Methods

• Systematic search of MEDLINE, EMBASE, and PsycINFO

• Included studies of subjects with non-affective psychosis or an at-risk mental state, first episode of illness (either first treatment contact or illness duration up to 5 years), and ≤ 2 weeks of antipsychotic treatment and healthy controls

• Physical comorbidities that may affect glucose homeostasis or pancreatic function were excluded
Primary outcome measures were:

- Fasting glucose
- Oral glucose tolerance test (OGTT)
- Fasting insulin
- Homeostatic model assessment of insulin resistance (HOMA-IR)
- Group differences were analyzed as standardized mean differences using Hedges $g$
- Random effects models were used for the meta-analysis
Study Results

• 16 case-control studies, with 731 patients and 614 controls, were included

• Fasting glucose was significantly higher in FEP patients vs controls (effect size, 0.20; 95% CI, 0.02-0.38)

• Plasma glucose after OGTT was also significantly higher in FEP patients vs controls (effect size, 0.61; 95% CI, 0.16-1.05)

• Fasting insulin was significantly higher in FEP patients vs controls (effect size, 0.41; 95% CI, 0.09-0.72)

• The HOMA-IR was also significantly higher in FEP patients vs controls (effect size 0.35; 95% CI, 0.14-0.55)
Study Results (continued)

- Only hemoglobin A1c was not altered in FEP patients vs controls.
- These associations were largely unchanged in secondary analyses of drug-naive subjects, as well as studies matching for ethnicity, BMI, and diet and exercise parameters, with the exception of fasting glucose in BMI-matched samples.
Discussion

• There is evidence for alterations in glucose homeostasis at the time of illness onset in psychosis with small to medium effect sizes

• Findings extend previous work showing an increased prevalence of type 2 diabetes in chronic schizophrenia

• Importantly, differences in BMI, diet, and exercise did not account for these associations
• Prospective studies of the effect of lifestyle factors on glucose dysregulation in FEP would be helpful

• Longitudinal studies of pharmacologic and lifestyle interventions in subjects with FEP and abnormal glucose metabolism are also warranted

• Clinicians must be aware that early psychosis represents a vulnerable phenotype for type 2 diabetes, and associated monitoring and interventions are needed


