Hyperlipidemia Correlated with Better Neurocognition in Patients with Schizophrenia

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Background

Cognitive dysfunction is a core feature of schizophrenia and is associated with functional dysfunction. Antipsychotic-induced dyslipidemia is a well-known phenomenon, and some studies suggest that dyslipidemia may be associated with the disease state of schizophrenia itself. It is generally believed that metabolic abnormalities may impair neurocognition in schizophrenia.

Objective

This study aimed to analyze prospective data from the NIMH-funded schizophrenia CATIE trial to examine the effects of hyperlipidemia on neurocognitive measures.

Methods

The CATIE Schizophrenia Trial was a national, prospective study examining the effectiveness of antipsychotic drugs. Screening data were collected on 1,460 patients, including demographics, psychiatric history, and metabolic variables. Serum cholesterol and triglycerides were measured in a subsample (n = 741) who were in a fasting (≥ eight hours) state. Neurocognition was assessed at baseline using the Neurocognitive Composite (NC) Score, an average of five composite subscale z-scores: 1) Processing Speed 2) Verbal Memory 3) Vigilance Summary Score 4) Reasoning Summary Score 5) Working Memory Summary Score. Regression and analysis of variance models (ANOVA) were used to examine the relationships between metabolic variables and neurocognition.

Results

The patients ranged in age from 18 to 67, with a mean (SD) age of 40.4 (11.0) years, and were more likely to be white (61%), non-Hispanic (89%), and male (75%). Patients with low high-density lipoprotein (HDL) cholesterol levels had significantly lower NC scores than patients with high HDL levels (p = 0.04). Conversely, patients with high total cholesterol had significantly higher NC scores than patients with low total cholesterol (p = 0.002). Participants with high triglycerides had significantly higher NC scores when compared to those with low triglycerides (p = 0.02). The results of the regression analyses, with the metabolic variables included as continuous variables in separate models, showed that higher total cholesterol significantly predicted higher NC (p < 0.0001). An exploratory analysis looking at other predictors of neurocognition found that prior duration of psychiatric illness, as measured by years since first antipsychotic medication prescribed, significantly predicted NC scores (p < 0.0001).

					Subscale p-values				
Risk factor	Risk Factor(s) Neuro Composite Mean (SD)*	No Risk Factor(s) Neuro Composite Mean (SD)*	Neuro Composite p-value	Adjusted effect size	Verbal Memory	Vigilance	Processing Speed	Reasoning	Working Memory
BMI, ≥ 25 kg/m²	0.008 (0.993)	-0.029 (1.030)	0.24						
Waist circumference, > 102 cm (men) or > 88 cm (women)	-0.050 (0.995)	0.040 (1.000)	0.37						
Hypertension, sys ≥ 135 or dia ≥ 85 mmHg	-0.045 (0.973)	0.024 (1.016)	0.47						
HDL cholesterol, < 40 mg/dL (men) or < 50 mg/dL (women)	-0.027 (0.984)	0.024 (1.015)	**0.04**	-0.12	0.51	0.07	**0.008**	0.09	0.3
Total cholesterol, >240 vs. < 200 mg/dL (n = 925)	0.130 (0.938)	-0.080 (1.003)	**0.002**	0.24	0.09	0.12	**0.02**	**0.005**	**0.006**
Fasting glucose, ≥ 100 mg/dL (n = 673)	-0.079 (0.993)	0.098 (0.978)	0.32						
Fasting triglycerides, ≥ 150 mg/dL (n = 673)	0.146 (0.980)	-0.022 (0.980)	**0.02**	0.19	0.19	**0.04**	0.2	**0.02**	0.07

*raw means shown

Discussion

This study found that hyperlipidemia, including components HDL cholesterol, total cholesterol, and triglycerides, correlated with better neurocognition in patients with schizophrenia. These findings are contrary to the commonly held belief that high cholesterol and triglyceride levels – two components of the metabolic syndrome often seen in patients with schizophrenia – may correlate with poor cognition in this population. While having high levels of cholesterol may contribute to an individual's cardiovascular risk, evidence that elevated lipid levels may in fact improve cognition in schizophrenia patients should be an important clinical consideration, particularly given that there are no current treatments for cognitive dysfunction in schizophrenia. Further research is necessary to elucidate ways in which cardiovascular risk can be mitigated in this population without further exacerbating neurocognitive deficits and the resulting functional dysfunction.

References

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