

# Chapter 3

## A Review of Electron Microscopy Studies of the Brain in Schizophrenia: In Search of Nanotoxicology From Air Pollution

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### ABSTRACT

*In previous work, the author demonstrated that two-thirds of the miRNA expressions associated with asbestos exposure in mesothelioma, especially the oncogenic miRNAs, are similarly expressed in schizophrenia brain tissue. No epidemiological evidence links schizophrenia to asbestos, a naturally occurring material often small enough to qualify as a nanoparticle (NP). This review investigated whether any microscopic study of brain tissue in schizophrenia observed inflammatory NPs of any chemical composition. Transmission electron microscopy (TEM) combined with x-ray energy dispersive spectroscopy is the accepted method for identifying the smallest NPs. However, the review found that no TEM study has used sufficient methods to identify NPs in schizophrenia brain tissue. The review also shows that schizophrenia risk is associated with urban air pollution and neuroinflammation and that NPs in urban air pollution can cause neuroinflammation. Research in this unexplored area of schizophrenia neuropathology may reveal new environmental exposures that might cause schizophrenia.*

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## **SCHIZOPHRENIA**

Schizophrenia is a severe mental disorder with a lifetime prevalence of approximately 0.3%–0.7%, usually beginning between the late teens and mid-30s and characterized by a range of cognitive, behavioral, and emotional symptoms associated with social and occupational dysfunction (Association, 2013; Uludag, 2024; D. M. Wang et al., 2022). No diagnostic tests for schizophrenia exist, but there is evidence of abnormalities in brain cellular architecture, gray matter volume, and white matter, as well as brain volume reductions (Association, 2013). The numerous risk factors for schizophrenia include genetic factors, season of birth, urban birth, pregnancy and birth complications affecting the fetus, stress, infection, migration, childhood adversity, cannabis use, and malnutrition (Association, 2013) (A. S. Brown, 2011; Lemvig et al., 2023; Robinson & Bergen, 2021).

### **MiRNA in Schizophrenia and Mesothelioma**

In previous work, I compared the expression of a subset of microRNAs (miRNA) in asbestos-related lung cancer/mesothelioma (ARLCM) to schizophrenia and glioma (J. S. Brown, Jr., 2023). At least 23 miRNAs are related to asbestos exposure in ARLCM, and the expressions of thirteen of these asbestos-related miRNAs are also reported in schizophrenia. The comparison found that schizophrenia shared identical expressions (up-regulated or down-regulated) with 69% of asbestos-related miRNA in ARLCM, compared with only 41% for glioma. Of 10 upregulated miRNAs in ARLCM, assumed to be oncogenic, seven were identically expressed in schizophrenia, but only two were identically expressed in glioma. This finding raised two questions: Why would schizophrenia have greater oncogenic similarity to ARLCM than glioma? Moreover, why would schizophrenia show any similarity to a foreign-body cancer?

### **TEM Studies of Brain Tissue in Schizophrenia**

To answer these questions, I first examined both the asbestos and schizophrenia literature for any epidemiological evidence suggestive of a relationship, but I found no such evidence. However, to rule out exposure to nano-size asbestos or any other nanoparticle (NP) in schizophrenia, I then examined ultrastructural studies of brain tissue in schizophrenia to determine if such investigations formally ruled out any NP exposure. I also intended to determine if any studies used techniques adequate

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