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**Letter to the Editor** *https://doi.org/10.18502/ijps.v20i3.19035*

# The Role of Metabolic Disorders in the Development of Waxy Flexibility in Patients with Catatonic Schizophrenia

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Dear Editor,

Catatonic schizophrenia, historically classified as a distinct subgroup of schizophrenia, is characterized by its own specific psychomotor disturbances, including symptoms such as catatonic flexibility. Research indicates that metabolic factors may intersect with neuropsychiatric pathways and influence symptoms like Waxy flexibility in catatonic schizophrenia (1).

Waxy flexibility is a motor sign that is deeply intertwined with catatonia, a neuropsychiatric syndrome characterized by disturbances in movement and behavior. This sign manifests as a slight resistance, even against passive positioning of the limbs, followed by the maintenance of the imposed posture, which is also referred to as catalepsy. It is typically observed alongside other catatonic symptoms such as stupor, mutism, and negativism. The pathophysiology of waxy flexibility primarily involves disturbances in neurotransmitter systems—particularly gamma-aminobutyric acid (GABA) and glutamate systems—which lead to impairments in motor control and behavioral regulation (2). However, despite these neurochemical insights, the complete etiological framework remains somewhat unclear, with metabolic factors recognized as significant contributors. Studies report that patients with schizophrenia are 2 to 3 times more likely to experience metabolic disorders compared to the general population, which plays a role in increasing the risk of cardiovascular diseases and premature mortality in these patients. This multifactorial relationship and the adverse metabolic side effects of antipsychotic medications, particularly second-generation antipsychotics, significantly impact weight gain and glucose homeostasis (3). Importantly, metabolic syndrome is associated not only with deteriorating physical health but also with neuropsychiatric complications that exacerbate psychiatric symptoms such as waxy flexibility (4).

The intersection between metabolic disorders and catatonic features like waxy flexibility likely involves several intertwined biological pathways. One hypothesis includes the effects of metabolic disorders on the central nervous system, particularly glucose and lipid metabolism disorders, which affect brain regions responsible for motor function and behavioral control. Metabolic changes induced by antipsychotics may alter hypothalamic homeostasis and impact the neurotransmitter systems and neural circuits involved in catatonia (5). Visceral obesity and insulin resistance also lead to neuroinflammation and microvascular changes that disrupt the cortical and subcortical pathways involved in motor regulation. This disruption may exacerbate existing neurological disorders in catatonia, such as reduced GABA-A receptor activity and impaired glutamate receptor function, consequently intensifying symptoms like waxy flexibility. Furthermore, the systemic effects of metabolic syndrome can create vulnerability to autonomic instability and muscular rigidity, thereby exacerbating the motor symptoms observed in catatonia (6). Additionally, metabolic abnormalities such as hyponatremia and rare metabolic disorders (like diabetic ketoacidosis and homocystinuria) have been introduced as potential triggers or modulators of catatonic symptoms. Although these specific metabolic conditions are less commonly seen in catatonia associated with schizophrenia, their presence underscores the broader biological plausibility of metabolic factors influencing waxy flexibility (7).

Understanding metabolic factors in catatonic schizophrenia, particularly in symptoms such as waxy

flexibility, is crucial for effective patient management. The high prevalence of metabolic syndrome necessitates routine screening and monitoring of patients with schizophrenia, especially those exhibiting catatonia or waxy flexibility. Early lifestyle interventions focusing on diet, physical activity, and smoking cessation can reduce cardiovascular risk and potentially improve overall clinical outcomes (8). The treatment of catatonia itself, often managed with benzodiazepines and electroconvulsive therapy (ECT), may be complicated by existing metabolic abnormalities that affect drug tolerance and side effects. For instance, physicians may need to exercise caution when prescribing antipsychotic medications that exacerbate metabolic disorders. Importantly, benzodiazepines, which enhance GABAergic activity involved in catatonia, remain first-line treatments and may even be effective in metabolically vulnerable patients (9).

## Conclusion

The waxy flexibility observed in catatonic schizophrenia reflects a complex interplay between neurological dysfunction and systemic metabolic disorders. Metabolic disturbances and related abnormalities not only impact the physical health of patients with schizophrenia but also significantly affect the biological neural substrates of catatonia and its motor manifestations, such as waxy flexibility. Understanding these metabolic effects underscores the necessity for integrated approaches to diagnosis, treatment, and long-term management, emphasizing metabolic screening and correction alongside targeted psychiatric interventions. By further elucidating the metabolic underpinnings of catatonic symptoms, new therapeutic strategies can be developed that may effectively improve the quality of life and prognosis for patients with catatonia in schizophrenia.

## Conflict of Interest

None.

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