Psychotropic medications and mitochondrial toxicity

Rebecca Anglin, Patricia Rosebush and Michael Mazurek

In a recent Review, Husseini Manji and colleagues summarize the growing body of evidence linking impaired mitochondrial function to the pathophysiology of several major psychiatric illnesses, including mood disorders, autism and schizophrenia (Impaired mitochondrial function in psychiatric disorders. *Nature Rev. Neurosci.* **13**, 293–307 (2012))¹.

One of the often-overlooked contributors to mitochondrial dysfunction is the psychotropic medication used to treat these psychiatric conditions. Multiple studies have shown that both typical and atypical antipsychotic medications can inhibit the mitochondrial respiratory chain^{2–4}. Similarly, the mood stabilizer valproic acid can inhibit the mitochondrial respiratory chain and result in secondary impairment of mitochondrial function through the induction of carnitine deficiency^{5,6}. Selective serotonin reuptake inhibitor antidepressants inhibit mitochondrial function in animal models of depression and are potentially toxic in high doses, resulting in dysfunction of the mitochondrial respiratory chain and decreased ATP production^{7,8}.

Psychiatric symptomatology can be the initial clinical expression of an underlying mitochondrial disorder^{9,10}. In our experience, the psychiatric symptoms of patients with mitochondrial disorders are often resistant to treatment and may actually worsen with exposure to psychotropic medications, supporting the notion that these agents can compromise mitochondrial function^{9,10}. This under-recognized mitochondrial toxicity may contribute to the limited efficacy and problematic side effects of many psychotropic medications, not only in those with mitochondrial disorders but also

in the much wider population of patients receiving treatment with these agents for psychiatric illness.

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Competing interests statement

The authors declare no competing financial interests.