May 2022

More on *T. gondii*

We reviewed the article by Dr. Torrey on *Toxoplasma gondii* (*T. gondii*) and schizophrenia ("Cats, toxoplasmosis, and psychosis: Understanding the risks," Current Psychiatry, May 2022, p. 14-19) with interest. Understanding infections in utero, during the perinatal period, and at other critical developmental stages may offer ways to prevent neurodevelopmental disorders. There appear to be good reasons to explore infectious and immune disruption of normal brain development. In a meta-analysis of 7 studies, Nayeri et al[1] found evidence to suggest *T. gondii* is a risk factor for autism spectrum disorder (ASD). Given the enormous loss of human potential and suffering resulting from schizophrenia and ASD, further exploration of toxoplasmosis and other infections may be valuable as we try to reduce the severe impact of these diseases.

The natural history of toxoplasmosis is an extraordinary example of nature's complexity. The life cycle of this parasite uses the nervous system of the mouse to increase its transmission. Behavior changes ranging from reduced cat urine avoidance and increased risk-taking are observed in mice infected with *T. gondii*.[2] Chronic toxoplasmosis may also affect human behavior.[3]

Cats are fascinating, complex creatures. Of note, they produce a protein structurally like the secretion of the slow loris.[4] The loris uses this brachial gland protein secretion as part of a defense strategy.[5] Consideration of a possible toxic, neuroimmune role of these small mammal proteins in psychiatric disorders may open other avenues to explore.[6]

Our relationship to domesticated animals has been connected to serious diseases throughout human history.[7] Severe acute respiratory syndrome and COVID-19 appear to be linked to animal reservoirs, mammals of the small animal trade, and the fur industry.[8,9] The rapid development of vaccines for COVID-19 is commendable. In conditions with multifactorial causation, managing an infectious component is worthy of consideration.

With mounting evidence suggesting a link between *T. gondii* and schizophrenia, ASD, and other diseases, further epidemiological studies and pilot interventions offer value. Interventions, including encouraging keeping cats indoors only, cat immunization, and human treatment, could be implemented in high-risk families. Efficacy requires data collection. While not easy, collaborative work by psychiatrists, developmental pediatricians, veterinarians, and epidemiologists is encouraged.

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Disclosures

The authors report no financial relationships with any companies whose products are mentioned in this letter, or with manufacturers of competing products.

Pramipexole for MDD

I appreciate Dr. Espejo's recommendations for treating patients who experience limited response from initial antidepressant therapy ("Treating major depressive disorder after limited response to an initial agent," Current Psychiatry,

October 2021, p. 51-53). I would like to add that pramipexole, a dopamine receptor agonist, can also alleviate depression. A meta-analysis concluded that patients receiving monotherapy or augmentation with pramipexole (mean maximum dose 1.62 mg/d) achieved response or remission of depression.[1] In an observational study of 116 patients with unipolar or bipolar depression, nearly 75% experienced response and 66% achieved remission with pramipexole augmentation (median maximum dose 1.05 mg/d).[2] Pramipexole is usually well-tolerated, although patients may experience nausea, somnolence, headache, and constipation, and they should be cautioned about the risk for compulsive behaviors and psychosis.

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doi: 10.12788/cp.0267