The complex relationship between neuropsychiatric disorders and infectious diseases: past, present, and the future of research

A complexa relação entre transtornos neuropsychiátricos e doenças infecciosas: o passado, o presente e o futuro das pesquisas

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DEAR EDITOR,

The current state of the COVID-19 pandemic has raised many concerns regarding indirectly and directly linked mental health disorders. Fear of infection, social isolation, and economic crisis have led to globally increased psychological distress. There has been some emerging evidence of neuropsychiatric sequelae related to COVID-19 since the SARS-CoV-2 virus can infect the brain. As a matter of fact, the relationship between infectious diseases and neuropsychiatric disorders is not a new theme of the discussion: along with history, it has been often observed and considered.

In a 1904 article, W.W. Ireland reported Ernst Siemerling’s (1857-1931) shared observations that many psychotic, manic, and depressive episodes were preceded by infectious diseases such as typhoid fever, pneumonia, and mumps. Siemerling discussed how those events seemed to be linked, and also commented that the “insanity outbreaks” preceded by infectious diseases seemed to be indistinguishable from the ones that weren’t preceded by an explicit infectious malady. As an example for all psychiatrists, Emil Kraepelin (1856-1926) was aware of a possible link between typhoid and scarlet fevers and psychiatric symptoms. Besides, Karl A. Menninger wrote in 1928 about how “schizophrenia syndrome” diagnosis could be a product of an infectious disease, such as influenza, for example.

Around the time of the “Spanish Flu” pandemic of the early 20th century, encephalitis lethargica (EL) emerged and spread worldwide. Constantin von Economo (1876-1931) coined the term in 1917 and was the first to describe it more precisely, as an inflammatory disorder of the CNS marked by hypersomnolence, psychosis, catatonia, and Parkinsonism. EL has a nonspecific prodromal phase, with influenza-like symptoms, and over months/years, the neuropsychiatric manifestations appeared, being notably similar to narcolepsy and idiopathic Parkinson’s Disease. It’s a supposition never proved that influenza caused EL, and given that, there have been some concerning comparisons between EL and COVID-19.

Nowadays, there has been evidence of neurological and psychiatric burden related not only to viral and bacterial infection but also parasitic infection caused by protozoan and platyhelminths. About research on the psychiatric field, it’s interesting to mention the lack of biomarkers. It’s intriguing how there is still much uncertainty about how to identify neuropsychiatric manifestations that could be related to infectious diseases. Research on the interactions between infectious and inflammatory processes could give more insight for neuropsychiatric nosology, as well as it may bring better comprehension of etiologic aspects in CNS disorders.

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Mental disorders emerge from a complex interplay between genetic, biochemical, psychosocial, and lifestyle factors, and a disruption in the central nervous system homeostasis caused by immune-inflammatory cascades could be one factor leading to the development of neuropsychiatric disorders.\textsuperscript{1,2,4} Considering the multifactorial aspects of neurotransmitter disbalances and neuroanatomic alterations on a more macro and/or micro-scale, it's reasonable to call for more investigation about the consequences of inflammatory processes caused by pathogenic agents in cognition and behavior. It seems like a possibility that some given neuropsychiatric diagnoses could be better managed by treating the infection and the inflammation process. Indeed, there is the need to strengthen warning about risk factors to prevent public health neuropsychiatric events.

**CONFLICTS OF INTEREST**

The authors report no conflicts of interest.

**REFERENCES**