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LETTERS TO THE EDITOR

Narcolepsy and COVID-19: sleeping on an opportunity?

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The coronavirus disease (COVID-19) has rapidly emerged as a global public health challenge. Although containing the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) remains foremost on the minds of many government agencies and private research foundations, the viral outbreak may also present a unique opportunity to better understand the association between immune challenge and the development of autoimmune conditions such as the neurologic sleep disorder narcolepsy.

People with type 1 narcolepsy experience a breakdown in the walls that separate sleep and wake. Their overnight sleep patterns are fragmented and often interleaved with periods of insomnia.[1] When awake, their consciousness is interrupted by strong, irresistible urges to nap, lapses in attention, and disconcerting intrusions of rapid eye movement sleep phenomena such as hypnagogic (dream-like) hallucinations and cataplexy (loss of voluntary muscle control).[1] Research over the last 2 decades has traced this clinical manifestation to the loss of a specific cell population seated within the lateral hypothalamus.[2,3] These cells produce hypocretin (orexin), which functions as a neurochemical regulator of arousal throughout the brain's wake-sleep circuitry.[3]

It is an open question as to why hypocretin-producing neurons degenerate in the brains of people with narcolepsy, although current hypotheses endorse the involvement of a wayward autoimmune reaction.[4,5] Nearly all individuals with type 1 narcolepsy—irrespective of ethnic and racial background—carry genetic variations in major histocompatibility genes that are essential for organizing T-cell responses to bacterial and viral infection.[4] In the wake of the 2009 H1N1 influenza pandemic, a surge of pediatric narcolepsy cases was reported in the People's Republic of China.[5] Northern European H1N1 vaccination efforts that year were also associated with a severalfold elevated risk of developing narcolepsy in children and young adults throughout Sweden, Finland, and Denmark.[5] These converging neurobiological, genetic, and epidemiologic data suggest that hypocretin neurons are somehow in the crosshairs of T cells activated by pathogenic antigens. Degeneration might occur through a process of mistaken identity (confusion of foreign vs host antigens) followed by T cell–mediated cytotoxicity, although this pathway has yet to be confirmed in people with narcolepsy.

The link between H1N1 response and/or vaccination and narcolepsy highlights an important translational medicine opportunity. The current COVID-19 pandemic may be a setting where interdisciplinary research can uncover further mechanistic insight into the early biological events that shape the development of narcolepsy in susceptible individuals. We would urge the scientific community and public health authorities to give greater scrutiny to new cases as they emerge in the current climate.

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