A real eye-opener: Narcolepsy bears classic autoimmune hallmarks

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Narcoleptics suffer from bouts of sleepiness and sleep attacks, which impair their ability to function in daily life. But the precise cause of narcolepsy has long eluded scientists, and the cure for the devastating neurological disorder afflicting an estimated three million people worldwide—and one in 3,000 Americans—remains at bay.

A new study published in Pharmacological Research by the world's leading autoimmune disease expert, Tel Aviv University's Prof. Yehuda Shoenfeld, finds that narcolepsy bears the trademarks of a classic autoimmune disorder and should be treated accordingly. The research, led by Prof. Shoenfeld, the Laura Schwarz-Kipp Chair for Research of

Autoimmune Diseases at TAU's Sackler Faculty of Medicine and Head of Zabludowicz Center for Autoimmune Diseases at Chaim Sheba Medical Center, Tel Hashomer, and conducted by doctoral student María-Teresa Arango, points to a particular autoimmune process as the trigger for the specific loss of orexin neurons, which maintain the delicate equilibrium between sleep and wakefulness in the brain.

Not just the genes

"Narcolepsy is interesting, because although it has been considered to be strictly genetic, it is induced by environmental factors, such as a burst of laughter or stress," said Prof. Shoenfeld. "Narcolepsy is devastating to those suffering from it and debilitating to children, in particular. There is no known therapy to treat it."

Narcolepsy first strikes people aged 10 to 25, plaguing them for life. Narcoleptics may experience any or all of the following symptoms: falling asleep without warning, anywhere, anytime, making it difficult to concentrate and fully function; excessive daytime sleepiness; the sudden loss of muscle tone; slurred speech or weakness of most muscles for a few seconds or a few minutes; a temporary inability to move or speak while falling asleep or upon waking; and hallucinations.

Prof. Shoenfeld first became interested in the subject after an avalanche of narcolepsy diagnoses swept Finland in 2009 following the administering of the H1N1 flu vaccine. "Following the H1N1 vaccine, 16 times the average incidence of narcolepsy was reported," said Prof. Shoenfeld.

Prof. Shoenfeld discovered that a group of researchers from the Sleep Control Project at the Tokyo Metropolitan Institute of Psychiatry in Japan had published a study on an autoantibody presence attacking tribbles, small granules in our brains containing regulatory orexin

neurons, which maintain the balance between sleep and wakefulness in the brain.

Fingering the culprit

"In patients and animals that develop narcolepsy, we have seen an evident depletion of orexin in the brain, and therefore a lack of balance, and later attacks of narcolepsy," said Prof. Shoenfeld. "Why is the orexin disappearing? We think the culprit is an autoimmune reaction—the binding of autoantibodies to the tribble granules to destroy them."

For the purpose of the new study, Prof. Shoenfeld and his team collaborated with the Japanese research group led by Dr. Makoto Honda to isolate the specific antibodies. These antibodies were then injected directly into laboratory mice. Ms. Arango monitored their behavior for several months, tracking their sleep patterns. "What we saw was an increased number of sleep attacks and irregular patterns of sleep in mice," said Prof. Shoenfeld. "Mice fall asleep like dogs, circling around before going to sleep. Suddenly, in this experiment, the mice just dropped off to sleep and then, just two minutes later, woke up as though nothing had happened.

"Our hope is to change the perception and diagnosis of narcolepsy, to define it as the 81st known autoimmune disease, because a better understanding of the mechanism causing this disease, which debilitates and humiliates so many people, will lead to better treatment and, maybe one day, a cure," Prof. Shoenfeld says. He is currently collaborating with Dr. Honda and his team to locate the area of the brain to which the targeting autoantibodies bind.

Provided by Tel Aviv University

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