Genetic association and autoimmunological mechanisms of narcolepsy

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Abstract: Narcolepsy is a lifelong sleep disorder characterized by excessive daytime sleepiness, cataplexy, hypnagogic hallucinations, and disturbed nocturnal sleep. Narcolepsy is caused by the loss of hypocretin (orexin)-producing neurons in the lateral hypothalamus. Evidence, such as a strong association with HLA DQB1*06:02, strongly suggests an autoimmune basis targeting hypocretin neurons. Genome-wide association studies have strengthened the association between narcolepsy and immune system gene polymorphisms, including the identification of polymorphisms in the T cell receptor alpha locus, TNFSF4 (also called OX40L), Cathepsin H (CTSH) the purinergic receptor P2RY11, and the DNA methyltransferase DNMT1. More recently, narcolepsy was identified in association with seasonal streptococcus, H1N1 infections in 2010 following the 2009 H1N1 pandemic (pH1N1) in China and following AS03-adjuvanted pH1N1 influenza vaccination in Northern Europe. How the immune system may be involved in disease initiation and/or progression remains a challenge to researchers. Potential immunological pathways that could lead to the specific elimination of hypocretin producing neurons, and are likely a combination of genetic and environmental factors, such as upper airway infections.
Keyword: Narcolepsy, H1N1, Gene, Hypocretin