|  |
| --- |
| KDM3A |
| Url: https://pubmed.ncbi.nlm.nih.gov/37553546 DOI: https://doi.org/10.1007/s10571-023-01391-z  Title(2023): Sleep Disorder Kleine-Levin Syndrome (KLS) Joins the List of Polygenic Brain Disorders Associated with Obstetric Complications.  Kleine-Levin Syndrome is a rare neurological disorder with onset typically during adolescence that is characterized by recurrent episodes of hypersomnia, behavioral changes, and cognitive abnormalities, in the absence of structural changes in neuroimaging. As for many functional brain disorders, the exact disease mechanism in Kleine-Levin Syndrome is presently unknown, preventing the development of specific treatment approaches or protective measures. Here we review the pathophysiology and genetics of this functional brain disorder and then present a specific working hypothesis. A neurodevelopmental mechanism has been suspected based on associations with obstetric complications. Recent studies have focused on genetic factors whereby the first genome-wide association study (GWAS) in Kleine-Levin Syndrome has defined a linkage at the TRANK1 locus. A Gene x Environment interaction model involving obstetric complications was proposed based on concepts developed for other functional brain disorders. To stimulate future research, we here performed annotations of the genes under consideration for Kleine-Levin Syndrome in relation to factors expected to be associated with obstetric complications. Annotations used data-mining of gene/protein lists related to for hypoxia, ischemia, and vascular factors and targeted literature searches. Tentative links for TRANK1, four additional genes in the TRANK1 locus, and LMOD3-LMO2 are described. Protein interaction data for TRANK1 indicate links to CBX2, CBX4, and KDM3A, that in turn can be tied to hypoxia. Taken together, the neurological sleep disorder, Kleine-Levin Syndrome, shows genetic and mechanistic overlap with well analyzed brain disorders such as schizophrenia, autism spectrum disorder and ADHD in which polygenic predisposition interacts with external events during brain development, including obstetric complications. |