Introduction

Human being need to rest on a daily basis. Lack of rest leads to severe physical and psychological symptoms which can lead to behavioral inactivity. Pathobiology and molecular mechanisms involved in sleep is quite complex and least understood phenomenon according to many researchers. Sleep studies and researches has gained a lot of momentum in recent years. The main reason is role of genetic background which can disrupt sleep and thereby causing several types of sleep disorders reported in literature till date [1].

Variation of sleep phenotypes, their intra-individual stability as well as familial aggregation of certain sleep related disorders has drawn a lot of attention recently. Human sleep EEG showed evidence that it is dependent on genetic background of the individual. EEG done in human sleep showed strong influence of genetic factors. A handful of familial analyses involving specific gene loci and twin studies has been done in this regard. In this review article focused discussion on genetic contribution to sleep phenotypes, twin and familial linkage studies and effect of genetic variation on sleep will be covered.

Previously twin studies has reported higher concordance of sleep habits, e.g. sleep duration and quality in monozygotic (MZ) than in dizygotic (DZ) twins, even when exposed to different environmental situation with an estimated heritability of 30%-44% [15-19]. Pittsburgh Sleep Quality Index (PSQI) is usually used to investigate subjective sleep quality [20]. Zung, et al. performed the first polysomnogram in MZ showing temporal sleep patterns in terms of sleep stages [21]. Genetic background contributes heavily on numerous sleep traits like sleep duration, quality, onset latency, efficiency and wake after sleep onset, REM/NREM sleep characteristics, stage changes, diurnal preference, behavioral reaction due to sleep loss, insomnia and several sleep related disorders like restless leg syndrome [22-25].

NREM sleep is found consistently to be under strong genetic control in humans and animal models as compared to REM sleep [26-28]. REM sleep amount was found to be significantly
correlated in MZ twins, 95% heritable in some studies, with conflicting results from other studies [21,23,25,29], sleep onset latency in MZ only [29], sleep efficiency and wake after sleep onset [18,19,24,29,30], stage changes and frequency profiles also in MZ [4,31], diurnal preference [19,32,33], neurobehavioral reaction to sleep loss [24], disorders like insomnia [19,34,35], RLS [36,37], sleep talking, bruxism, enuresis [38-40].

In terms of familial and linkage studies certain sleep-related diseases show high familial risk and specific modes of transmission, loci and certain molecules.

**Familial Advanced Sleep Phase Syndrome (FASPS)**

It shows an AD pattern of inheritance, characterized by persistent early evening sleep onset and early morning awakening. Although the complaint of awakening earlier than desired is relatively common, particularly in older adults, extreme advance of sleep phase is rare. hPer2, CK1ε, and CK1δ has been associated with this syndrome complex [41,42]. The circadian rhythms of sleep propensity and melatonin secretion are regulated by a central circadian clock, most importantly the suprachiasmatic nucleus of the hypothalamus along with body core temperature. Reid, et al. used measures of sleep onset and offset, dim light melatonin onset, Home-Ostberg morningness - evenningness questionnaire and clinical interviews in a 32 member family with ASPS [43].

Autosomal semi-dominant mutations in rodents with fast or slow biological clocks (i.e. short or long endogenous period lengths; tau) are associated with phase-advanced or delayed sleep-wake rhythms, respectively [44]. A known missense mutation (bp2106 A/G) in hPer2 was checked in 2 Japanese families. None of the tested subjects possessed the missense mutation and there was no significant linkage between affected subjects with hPer2 region by 2-point mapping and by direct sequencing of 23 exons of hPer2, supporting the possibility of genetic heterogeneity [45]. Phosphorylation of PER proteins regulates their stability as well as their subcellular localization. Vanselow, et al. have identified 21 phosphorylated residues of mPER2 including Ser 659, which is mutated in patients suffering from FASPS. Phosphorylation at Ser 659 results in nuclear retention and stabilization of mPER2, whereas phosphorylation at other sites leads to mPER2 degradation in oscillating fibroblasts [46].

**Restless Legs Syndrome (RLS)**

Diagnostic criteria of RLS is quite simple [47]. Mode of inheritance can be AD, AR and few cases are not clear. AD type comprises of 5 types of RLS (1-5), sequenced to long and short arm of chromosome [48-52,53-58]. Liebetanz, et al. showed fine-mapping of an AD locus in a family of Bavarian origin with intrafamilial heterogeneity with RLS3 [59]. Desautels, et al. examined 276 individuals from 19 families using a selection of markers spanning the identified candidate interval on chromosome 12q. Results also suggested the presence of heterogeneity in RLS as linkage was formally excluded across the region in 6 pedigrees. Significantly higher periodic leg movements during sleep indices were observed for all probands with RLS from linked families showing AR pattern of inheritance of RLS1 [60], unclear inheritance pattern in RLS2(12q,14q) and related to several other molecules like MEIS1.

Sarayloo, et al. used human cell lines to conduct a RNA-Seq study. MEIS1, acts as a regulator of the expression of many other genes and some of the genes affected by its expression level are linked to pathways previously reported to be associated with RLS. Cells where MEIS1 expression was either increased or prevented, bone mineral absorption was the principal dysregulated pathway. The mineral absorption main pathway genes, HMOX1 and VDR are involved in iron metabolism and response to vitamin D, respectively. Same enrichment of the mineral absorption pathway in postmortem brain tissues of RLS patients showed a reduced expression of MEIS1. Expression of genes encoding metallothioneins (MTs) was observed to be dysregulated across the RNA-Seq datasets generated from both human cells and tissues in their study. MTs are highly relevant to RLS as they bind intracellular metals, protect against oxidative stress and interact with ferritins which manage iron level in the central nervous system. While MTs have been implicated in the pathogenesis of neurodegenerative diseases such as Parkinson’s disease this was the first study showed the molecular association with RLS [61,62].

RLS-linked genetic signal has been mapped to an intronic regulatory element within MEIS1. This element plays a role in the ganglionic eminences of the developing forebrain, with the RLS risk allele related to a reduced activation of the enhancer part. Ganglionic eminences play an important role in the development of genetic susceptibility to RLS. Some rare variants within MEIS1 alone are sufficient to suppress MEIS1 function in neural development, providing further evidence of the importance of neurodevelopmental processes in the pathological mechanism of MEIS1 in RLS. Salminen, et al. 2019 reported heterozygous MEIS1 inactivation in mice causing hyperactivity at the onset of the inactive period, consistent with human RLS. These mice related animal study also revealed an effect of MEIS1 on the dopaminergic system at both the spinal and supraspinal level thereby suggesting complex pathomechanistic process [63], BTBD9, MAP2K5, LBOXCOR1, DMT1 [64-68]. Recently Tilch, et al. has updated the genetic profile of RLS by mutation load analysis previously not reported [69]. TOX3 gene variant could be associated with painful restless legs [70].

**Primary Nocturnal Enuresis (PNE)**

Nocturnal enuresis, or nightly bedwetting in children more than seven years of age affects about 10% of seven-year-old
children, with a wide range of frequencies between populations. From the age of seven there is a spontaneous cure rate of 15% per year, such that few remain affected even after the age of 16 years. Two types of nocturnal enuresis exists: type I (PEN1, primary) with at least three nightly episodes in children above seven years, where the child has always had the disorder and type II (secondary) where the child has been dry for at least six months, but enuresis has recurred. Reports from a Danish family population, in which 17 families were examined, eleven of these family had type I nocturnal enuresis (PEN1) that appeared to follow an AD mode of inheritance with penetrance almost above 90%. Strong evidence of linkage with the DNA polymorphisms D13S291 and D13S263 was found. Multipoint analysis indicated that these markers flank the disease locus at chromosome 13q13-q14.3 as reported by Eiberg et al. [71-73]. Arnell, et al. found a region around D12S80 on chromosome 12q that showed a positive two point lod score in six of the families among sixteen of them. Ratio of males to females was 3:1, indicating sex linked or sex influenced factors [74].

Linkage analysis revealed 6 families with dominant primary nocturnal enuresis around the aquaporin-2 (AQP2) water channel locus. PNE is ameliorated by desmopressin, AQP2 expression is increased by desmopressin and AQP2 is essential for concentrating urine. Deen, et al. in their study reported no mutation in the AQP2 coding, the AQP2 gene is excluded as a candidate for autosomal dominant PNE in these families in which the disease co-segregates with chromosome 12q [75]. Eiberg, et al. in their research used total genome scan and multipoint analysis and mapped PNE to chromosome 22 between the markers D22S446 and D22S343 with a multipoint lod score of 4.51. GNAZ has a transducin function in eye and brain and is an obvious candidate gene on chromosome 22q11 for PNE [76].

Brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) are neurotrophins which affects maturation of the nervous system. Delayed neuronal maturation has been suggested as a pathogenetic mechanism in primary monosymptomatic nocturnal enuresis (PMNE). Neurotrophin gene polymorphisms did not significantly contribute to the development of PMNE, but urine levels of neurotrophin gene products were higher in PMNE [77]. Dopamine D4 receptor (DRD4) promoter (-616; rs747302) has been associated with primary nocturnal enuresis (PNE). Yu, et al. reported C-allele carriers were associated with a higher AS (Arousal from Sleep), decreased GMV (Grey Matter Volume) and FCD (Functional Connectivity Density) in the pregenual anterior cingulate cortex. Children with PNE carrying the C-allele exhibit decreased GMV and FCD in the thalamus however, controls who participated in the studies carrying the C allele exhibit increased FCD in the posterior cingulate cortex. Thus this genetic variation of the DRD4 locus may give a genetic susceptibility of the DRD4 -616 C allele to PNE [78,79]. Fatouh, et al. reported PNE can be in part linked to reversed ADH circadian rhythm which may be linked to chromosome 22 [80]. The association between 5HTR2A gene polymorphisms and polysymptomatic NE was reported by Wei, et al. suggesting that genetic variations at 5HTR2A may influence NE treatment response [81].

Genetic variations affecting sleep phenotypes include several genes, modifications like SNP, missense mutation, VNTR, insertion/deletion variant, SNPs in promoter and coding region, missense mutation in signal peptide, SNP in 5’UTR. Specific genes are described below:

**CLOCK:** A transcription-translation feedback loop serves as the basic mechanism for the clock machinery in the suprachiasmatic nucleus (SCN) to control circadian rhythmicity. The PER and CRY proteins, in turn, act as negative regulators of CLOCK/ BMAL1 activity by forming a repressor complex with casein kinase (CK) 1ε (encoded by the CSNK1E gene) and CK1δ (CSNK1D) [52,59]. Besides their function in circadian rhythmicity, clock genes have also been found to influence sleep variables. Supporting evidence comes from animal models showing that knockout of BMAL1 and NPAS2 and double knockout of Cry1 and Cry2 lead to abnormalities in sleep homeostasis in animal model [82-84]. In 1998, Katzenberg, found a T3111C polymorphism in the 3’ UTR of CLOCK associated with diurnal preferences, in that carriers of the C-allele are more often evening-type. In a Japanese sample, the highest eveningness was likewise found in C/C homozygous subjects, along with significantly delayed sleep onset, shorter sleep duration, and higher daytime sleepiness compared with either heterozygous or homozygous T-allele carriers [85-93].

**SLC6A3(DAT):** In humans, a VNTR polymorphism in the 3’ UTR of the DAT encoding gene SLC6A3 leads to less DAT in the striatum in individuals homozygous for the long 10-repeat allele as compared with carriers of the 9 repeat allele. According to the available animal data, 10/10 carriers are more sensitive to caffeine generally, as well as to its effect on reducing SWS rebound after sleep deprivation, which was found more pronounced in 10- repeat homozygotes [94-98].

**MAOA:** Monoamine oxidase (MAO) A and B are encoded on the X- chromosome and catalyze the degradation of serotonin and melatonin. Females carrying an allele conferring higher activity due to a variable number tandem repeat (VNTR) polymorphism in the MAO- A promoter region are at higher risk of developing RLS. The less active allele seems to confer susceptibility to depression and poor sleep quality. Koch, et al. proposed an association of a VNTR in intron 1 of the MAOA gene and a dinucleotide repeat in intron 2 of the MAOB gene with the occurrence of narcolepsy with cataplexy. MAO- A and - B inhibitors are capable of reducing symptoms of narcolepsy such as cataplexy and abnormal REM sleep [99-102,103-106].

**ADA:** Adenosinergic neurotransmission is suspected to play a major role in the regulation of sleep and wakefulness and their homeostasis in mice and humans. Retey, et al. found...
an increase in slow wave sleep (SWS) during an undisturbed night in ADA* 1–2 carriers resembling the effects of one night of sleep deprivation [107]. This was further accompanied by higher delta power in NREM sleep, which is a marker of sleep need [108-112].

**BDNF:** Evidence in the recent past suggested increased sleep slow waves after sleep deprivation is a reflection in plastic synaptic processes, and that brain-derived neurotrophic factor (BDNF) is causally involved in their homeostatic regulation. The functional Val66Met polymorphism of the gene encoding pro-BDNF causes impaired activity-dependent secretion of mature BDNF protein. Bachmann, et al. reported about the contribution of BDNF to the regulation of sleep slow wave oscillations and variation in neuronal plasticity modulates NREM sleep intensity in humans [113-124].

**PRNP:** FFI (Fatal Familial Insomnia) is characterized by disrupted sleep, i.e., loss of sleep spindles and slow wave sleep, and impaired sleep stage organization, as well as progressive reduction of sleep time. Reduced metabolism in thalamic and limbic regions and degeneration of thalamic nuclei has been identified. A missense mutation, a G→A transition at codon 178, leads to substitution of aspartate for asparagine. Two Italian affected kindreds revealed an underlying point mutation in the prion protein (PrP) gene (PRNP) on chromosome 20. Creutzfeldt-Jakob disease (CJD) is characterized by the same mutation and accumulation of protease-resistant prion protein plaques, but differs from FFI regarding a polymorphism at codon 129, which is common and leads to either incorporation of a methionine or valine and further to protein isoforms differing in size and glycosylation pattern. While in FFI-affected individuals the mutated allele encodes for methionine, those with CJD express valine on the mutated PRNP allele [125-130].

**ADORA:** Common genetic variation of ADORA2A is an important determinant of psychomotor vigilance in rested and sleep-deprived state. It also modulates individual responses to caffeine after sleep deprivation. Role for adenosine A (2A) receptors in the effects of prolonged wakefulness on vigilant attention and the sleep EEG [131]. Role of adenosine A2A receptors for sleep in humans, suggest that a common variation in the early morning. These effects appear to be mediated through homeostatic sleep pressure [142,143]. Individual phase differences in PER3 expression during a constant routine correlate with sleep timing during entrainment. PER3 expression in leukocytes represents a useful molecular marker of the circadian processes governing sleep-wake timing [93].

**COMT:** A sexual dimorphism and a strong effect of COMT genotype on severity of narcolepsy exists. Women narcoleptics with high COMT activity fell asleep twice as fast as those with low COMT activity during the multiple sleep latency test (MSLT) while the opposite was true for men. COMT genotype also strongly affected the presence of sleep paralysis and the number of REM sleep onsets during the MSLT [99]. Dopaminergic mechanisms contribute to impaired wakening functions after sleep loss [133]. The Val158Met polymorphism of COMT modulates the effects of modafinil on the NREM sleep EEG in recovery sleep after prolonged wakefulness. The sleep EEG changes induced by modafinil markedly differ from those of caffeine, showing that pharmacological interference with dopaminergic and adenosinergic neurotransmission during sleep deprivation differently affects sleep homeostasis [134,135].

**TNFA:** Three SNP of the TNFA promoter and one adjacent microsatellite was investigated by Wieczorek, et al. These results point towards an etiological influence of TNFA alleles in narcolepsy and support previous findings suggesting genetic heterogeneity and differences in pathophysiological characteristics of HLA-DR2 positive and negative narcolepsy [136]. TNF-alpha with 857T was associated with narcolepsy independent of the strong association of DRB1*1501 [137].

**PER3:** Polymorphism in the PER3 promoter associates with diurnal preference and delayed sleep phase disorder [138-140]. PER3 VNTR polymorphism was not associated with individual differences in neurobehavioral responses to PSD (Partial Sleep Deprivation), although it was related to one marker of sleep homoeostatic response during PSD. PER3 does not contribute to the neurobehavioral effects of chronic sleep loss [141]. PER3 polymorphism differentially influences the effects of sleep deprivation on executive and non-executive function in the early morning. These effects appear to be mediated through homeostatic sleep pressure [142,143]. Individual phase differences in PER3 expression during a constant routine correlate with sleep timing during entrainment. PER3 expression in leukocytes represents a useful molecular marker of the circadian processes governing sleep-wake timing [93].

**TNFR2:** In a Japanese case control study it was found TNFR2 is likely associated with the susceptibility to narcolepsy. Relationship of TNFR2 and TNF-alpha with the susceptibility to narcolepsy indicates the possibility that an additive effect on the susceptibility to the disorder lies between TNFR2-196R and TNF-alpha (-857T) alleles [144]. Chen, et al. reported increased TNF-α level was associated with narcolepsy in our patients, and that chronic inflammation due to various factors might have led to the increased TNF-α levels found in their patients [145].

**HCRT:** Hypocretin loci do not contribute significantly to genetic predisposition, however cases of human narcolepsy are associated with a deficient hypocretin system [146]. Hypocretin-specific CD8+ T cells was detected in the blood and cerebrospinal fluid of several patients in a study with narcolepsy [147]. Selective hypocretin receptor 2 agonist (YNT-185) has been shown to ameliorate symptoms of narcolepsy in murine models [148].

**GABRA (GABA A receptors):** A missense mutation was found in the gene of the beta3 subunit nucleotide polymorphism in a patient with chronic insomnia [149]. Pharmacogenetic experiments are currently leading to an understanding of the circuit mechanisms in the hypothalamus by which zolpidem and similar compounds induce sleep at...
α2β2γ2-type GABAA receptors [150]. GABA receptors undergo dynamic and differential changes in the wake-active Orx neurons and the sleep-active MCH neurons as a function of and homeostatic adjustment to their preceding activity and sleep-wake state [151].

**HTR2A (5-HT2A receptor):** Serotonin (5-HT) 5-HT2A receptor (5-HT2AR) and 5-HT2C receptor (5-HT2CR) in the central nervous system are implicated in a range of normal behaviors (e.g., appetite, sleep) [152]. Job stress and 5-HTR2A receptor gene polymorphisms are associated with sleep quality in physicians. Subjects with high job stress level or/and the -1438G/A GG genotype were more likely to report poor sleep quality, and furthermore, their combination effect on sleep quality was higher than their independent effects [153]. Polymorphisms of 5-HT 2A gene and obstructive sleep apnea was shown in metaanalysis [154,155]. Joëlle Adrien in one animal study showed the role of serotonin transmission in mice model [106].

**SLC6A4 (5-HTT):** Tryptophan improved objective sleep efficiency and objective wake after sleep onset irrespective of allelic variation in one study [156]. Tryptophan augmentation may be a valuable treatment strategy for sleep impairments related to genetic deficiencies in 5-HT functioning. A metaanalysis demonstrated that 5-HTR-1438 "A" and 5-HTTVNTR "10" alleles were significantly associated with OSAS. The "S" allele of 5-HTTLPR and the "GG" genotype of LEPR conferred protection against OSAS in line with some other researches [157-160].

**Discussion**

Sleep as we see is the most complex biological process in human beings. In this article genes associated with sleep is being reviewed in details.MZ are more affected than DZ as evident from the twin studies. Disorders associated with sleep genetics include insomnia, eating disturbances during sleep (i.e., sleep apnea), movement disorders during sleep (i.e., Restless leg syndrome, Periodic leg movements) and sleep-wake state dissociation disorders (i.e., narcolepsy, Rapid Eye Movement (REM) sleep Disorder, sleep walking).

Familial and linkage studies also hinted at several diseases like FASPS, RLS, and PNE. Pattern of inheritance can be AD/AR or of unclear origin. Several involved molecules and loci are reported among studies. Genes, modification at cellular level like SNP, VNTR, and missense mutations are also reported in literature and every gene modification can lead to different phenotypic trait related to sleep. Neurotransmitters like adenosine, dopamine, serotonin, GABA are involved along with individual effect and complex interaction among them related to neuroanatomical circuit. Molecules like MAO, COMT, TNF, BDNF, Prion protein, orexin, hypocretin are involved in sleep disorders associated with gene interaction. Circadian CLOCK genes are also reviewed in this article.

**Conclusion**

Genetics of sleep are still studied because it is considered as a very complex mechanism in humans. Sleep phenotypes and sleep disorders are controlled by individualised genetic factors. Mechanism of sleep function and pathophysiology behind it is controlled from molecular to organismic behavioral level. Sound sleep is important for proper functioning of individual. Improper sleep can lead to unnecessary stress and can be harbinger of diseases like hypertension, diabetes mellitus etc. and decreased neurocognitive status. Various genes are responsible for sleep disorders however if any single gene involved is not known yet. Sleep studies are quite complicated and even PSG may not be able to pick the diagnosis at initial stage. Genetic sequencing may be of great help in subset of population when diagnosis is not clear. Further studies are required in form of basic and translational research which will involve linking of various disorder phenotypes to normal mechanisms regulating the most basic biological substrates.

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**References**

1. Veatch OJ, Malow BA. Review of the Genetic Basis of Sleep and Sleep Disorders. JAMA Neurol. 2014; 71: 1058-1060.
2. van Beijsterveldt CEM, Molenaar PCM, de Geus EJC, Boomsma DI. Heritability of human brain functioning as assessed by electroencephalography. Am J Hum Genet. 1996; 58: 562-573. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/8644716
3. Landolt HP. Genetic determination of sleep EEG profiles in healthy humans. Prog Brain Res. 2011; 193: 51-61. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21854955
4. Ambrosius U, Lietzenmaier S, Wehrle R, Wichniak A, Kalus S, et al. Heritability of sleep electroencephalogram. Biol Psychiatry. 2008; 64: 344-348. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18405882
5. De Gennaro L, Marzano C, Fratello F, Moroni F, Pellicciani MC, et al. The electroencephalographic fingerprint of sleep is genetically determined: a twin study. Ann Neurol. 2008; 64: 455-460. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/1868819
6. Tafiti M, Petit B, Chollet D, Neidhart E, de Bilbao F, et al. Deficiency in short-chain fatty acid beta-oxidation affects theta oscillations during sleep. Nat Genet. 2003; 34: 343-348. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12796782
7. Maret S, Franken P, Dauvilliers Y, Ghyselinck NB, Chambon P, et al. Retinoic acid signaling affects cortical synchrony during sleep. Science. 2005; 310: 111-113. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16210540
8. Ashbrook LH, Krystal AD, Fu YH, Ptáček LJ. Genetics of the human circadian clock and sleep homeostat. Neuropsychopharmacology. 2020; 45: 45-54. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/31400754
Do genes matter in sleep? A comprehensive update

9. Frank MG. The mystery of sleep function: current perspectives and future directions. Rev Neurosci. 2006; 17: 375-392. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17139839

Mignot E. Why we sleep: the temporal organization of recovery. PLoS Biol. 2008; 6: e106. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18447584

Crockier A, Sehgal A. Genetic analysis of sleep. Genes Dev. 2010; 24: 1220-1235.

Cirelli C. The genetic and molecular regulation of sleep: from fruit flies to humans. Nat Rev Neurosci. 2009; 10: 549-560. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19617891

Linkowski P. EEG sleep patterns in twins. J Sleep Res. 1999; 8: 11-13. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10983259

Allada R, Siegel JM. Unearthing the phylogenetic roots of sleep. Curr Biol. 2008; 18; R670-R679. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18682212

Partinen M, Kaprio J, Koskenvuo M. Genetic and environmental determination of human sleep. Sleep. 1983; 6: 179-185. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/6684786

Gedda L, Brenci G. Twins living apart test: progress report. Acta Genet Med Gemellol (Roma). 1983; 32: 17-22. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/6684862

Hublin C, Partinen M, Koskenvuo M, Kaprio J. Heritability and mortality risk of insomnia- related symptoms: a genetic epidemiologic study in a population- based twin cohort. Sleep. 2011; 34: 957-964. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21731146

Rao WW, Li W, Qi H. Sleep quality in medical students: a comprehensive meta-analysis of observational studies. Sleep Breath. 2020; 10. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/32072469

Zung WW, Wilson WP. Sleep and dream patterns in twins. Markov analysis of a genetic trait. Adv Biol Psychiatry. 1966; 9: 119-130. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/4300786

Linkowski P, Kerkhofs M, Hauser J. Recent developments in EEG sleep. a study in twins living apart. Electroencephalogr Clin Neurophysiol. 1991; 79: 114-118. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/1713824

Linkowski P, Kerkhofs M, Hauspie R. Genetic determinants of EEG sleep: a study in twins living apart. Electroencephalogr Clin Neurophysiol. 1989; 73: 279-284. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/2477214

Kuna ST, Maislin G, Pack FM. Heritability of performance deficit accumulation during acute sleep deprivation in twins. Sleep. 2012; 35: 12231233. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22942500

Barclay NL, Gregory AM. Quantitative genetic research on sleep: a review of normal sleep, sleep disturbances and associated emotional, behavioural, and health- related difficulties. Sleep Med Rev. 2013; 17: 29-40. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22560641

Linkowski P. EEG sleep patterns in twins. J Sleep Res. 1999; 8: 11-13.

Tafti M, Franken P, Kitahama K. Localization of candidate genomic regions influencing paradoxical sleep in mice. Neuroreport. 1997; 8: 3755-3758. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9427364

Franken P, Chollet D, Tafti M. The homeostatic regulation of sleep need is under genetic control. J Neurosci. 2001; 21: 2610-2621. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11306614

Webb WB, Campbell SS. Relationships in sleep characteristics of identical and fraternal twins. Arch Gen Psychiatry. 1983; 40: 1093-1095. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/6684906

Boomsma DI, Van Someren EJ, Beem AL. Sleep during a regular week night: a twin- sibling study. Twin Res Hum Genet. 2008; 11: 538-545. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18828737

De Gennaro L, Ferrara M, Vecchio F. An electroencephalographic fingerprint of human sleep. Neuroimage. 2005; 26: 114-122. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15862211

Hur YM. Stability of genetic influence on morningness- eveningness: a cross- sectional examination of South Korean twins from preadolescence to young adulthood. J Sleep Res. 2007; 16: 17-23. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17309759

Koskenvuo M, Hublin C, Partinen M. Heritability of diurnal type: a nationwide study of 8753 adult twin pairs. J Sleep Res. 2007; 16: 156-162. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17542945

Drake CL, Friedman NP, Wright KP, Jr, Roth T. Sleep reactivity and insomnia: genetic and environmental influences. Sleep. 2011; 34: 1179-1188. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21886355

Watson NF, Goldberg J, Arguelles L, Buchwald D. Genetic and environmental influences on insomnia, daytime sleepiness, and obesity in twins. Sleep. 2006; 29: 645-649. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16774154

Xiong L, Jang K, Montplaisir J. Canadian restless legs syndrome twin study. Neurology. 2007; 68: 1631-1633. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17485653

Desai AV, Cherkas LF, Spector TD, Williams AJ. Genetic influences in self- reported symptoms of obstructive sleep apnoea and restless legs: a twin study. Twin Res. 2004; 7: 589-595. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15507009

Hublin C, Kaprio J, Partinen M, Koskenvuo M. Sleep talking in twins: epidemiologic and psychiatric comorbidity. Behav Genet. 1998; 28: 289-298.

Hublin C, Kaprio J, Partinen M, Koskenvuo M. Sleep bruxism based on self- report in a nationwide twin cohort. J Sleep Res. 1998; 7: 61-67. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9613429

Hublin C, Kaprio J, Partinen M, Koskenvuo M. Nocturnal enuresis in a nationwide twin cohort. Sleep. 1998; 21: 579-585. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9779517

Toh KL, Jones CR, He Y. An hPer2 phosphorylation site mutation in familial advanced sleep phase syndrome. Science. 2001; 291: 1043-1043. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11232563

Xu Y, Padiath QS, Shapiro RE. Functional consequences of a CK1δ mutation causing familial advanced sleep phase syndrome. Nature. 2005; 434: 640-644. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15800623

Reid KJ, Chang AM, Dubocovich ML, Turek FW, Takahashi JS, et al. Familial advanced sleep phase syndrome. Arch Neurol. 2001; 58: 1089-1094. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11448298

Jones CR, Campbell SS, Zone SE. Familial advanced sleep-phase syndrome: A short-period circadian rhythm variant in humans. Nat Med. 1999; 5: 1062-1065. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10470086

https://doi.org/10.29328/journal.jnnd.1001029

https://www.heighpubs.org/jnnd
50. Caylak E. The genetics of sleep disorders in humans: narcolepsy, restless legs syndrome maps on chromosome 14q. Brain. 2003; 126: 1485-1492.

51. Winkelmann J, Muller MB. Genetics of restless legs syndrome: a novel autosomal dominant locus in a family with intrafamilial heterogeneity. Mov Disord. 2006; 21: 1189-1195. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16685686

52. Vogl FD, Pichler I, Adel S. Restless legs syndrome: epidemiological and clinicogenetic study in a South Tyrolean population isolate. Mov Disord. 2006; 21: 1189-1195. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16983144

53. Von GA, Eiberg H, Hollmann E. Molecular genetics of nocturnal primary enuresis on chromosome 22q11. Eur Urol. 1998; 33: 344-347. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9599735
Do genes matter in sleep? A comprehensive update

77. Ece A, Coşkun S, Şahin C, Tan I, Karabel D, et al. BDNF and NGF gene polymorphisms and urine BDNF-NGF levels in children with primary monosymptomatic nocturnal enuresis. J Pediatr Urol. 2019; 15: 255.e1-255.e7. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/30981636

78. Yu B, Chang N, Lu Y, Ma H, Liu N, et al. Effect of DRD4 receptor -616 C/G polymorphism on brain structure and functional connectivity density in pediatric primary nocturnal enuresis patients. Sci Rep. 2017; 7: 1226. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/28450726

79. Dai XM, Ma HW, Lu Y, Pan XX. Relationship between dopamine D4 receptor gene polymorphisms and primary nocturnal enuresis. Zhongguo Dang Dai Er Ke Za Zhi. 2008; 10: 607-610. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18947481

80. Fatouh AA, Motawie AA, Abd Al-Aziz AM. Anti-diuretic hormone and genetic study in primary nocturnal enuresis. J Pediatr Urol. 2013; 9: 831-837. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23246575

81. Wei CC, Wan L, Lin WY, Tsai FJ. Rs 6313 polymorphism in 5-hydroxytryptamine receptor 2A gene association with polymysymptomatic primary nocturnal enuresis. J Clin Lab Anal. 2010; 24: 371-375. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21089166

82. Wisor JP, O'Hara BF, Terao A. A role for cryptochromes in sleep regulation. BMC Neurosci. 2002; 3: 20. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12495442

83. Franken P, Dudley CA, Estill SJ. Npas2 as a transcriptional regulator of non-rapid eye movement sleep: genotype and sex interactions. Proc Natl Acad Sci USA. 2006; 103: 7118-7123. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16636276

84. Laposky A, Easton A, Dugovic C. Deletion of the mammalian circadian clock gene BMAL1/ Mop3 alters baseline sleep architecture and the response to sleep deprivation. Sleep. 2005; 28: 395-409. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16171284

85. Katzenberg D, Young T, Finn L. A CLOCK polymorphism associated with human diurnal preference. Sleep. 1998; 21: 569-576. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9779516

86. Mishima K, Tozawa T, Satoh K. The 3111T/C polymorphism of hClock is associated with evening preference and delayed sleep timing in a Japanese population sample. Am J Med Genet B Neuropsychiatr Genet. 2005; 138B: 101-104. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15578592

87. Morris AR, Stanton DL, Roman D, Liu AC. Systems Level Understanding of Circadian Integration with Cell Physiology. J Mol Biol. 2020. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/32061938

88. Hor CN, Yeung J, Jan M, et al. Sleep-wake-driven and circadian contributions to daily rhythms in gene expression and chromatin accessibility in the murine cortex. Proc Natl Acad Sci USA. 2019; 116: 25773-25783. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/31776259

89. Charrier A, Olliac B, Roubertoux P, Tordjman S. Clock Genes and Altered Sleep-Wake Rhythms: Their Role in the Development of Psychiatric Disorders. Int J Mol Sci. 2017; 18: 938. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/28468274

90. Von Schantz M, Archer SN. Clocks, genes and sleep. J R Soc Med. 2003; 96: 486-489. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14519724

91. Langford D, Shostak A, Oster H. Clock genes and sleep. Pflugers Arch. 2012; 463: 3-14. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21833490

92. Comasco E, Nordquist N, Göktürk C. The clock gene PER2 and sleep problems: association with alcohol consumption among Swedish adolescents. Ups J Med Sci. 2010; 115: 41-48. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20187847

93. Archer. Inter-Individual Differences In Habitual Sleep Timing and Entrained Phase of Endogenous Circadian Rhythms of BMAL1, PER2 and PER3 mRNA in Human Leukocytes. Sleep. 2008; 31: 608-617. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18517031

94. Holst SC, Bersaglieri A, Bachmann V. Dopaminergic role in regulating neurophysiological markers of sleep homeostasis in humans. J Neurosci. 2014; 34: 566-573. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24403155

95. Rhodes JA, Lane JM, Vlasac IM, Rutter MK, Czeisler CA, et al. Association of DAT1 genetic variants with habitual sleep duration in the UK Biobank. Sleep. 2019; 42: zsy193. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/30299516

96. Satterfield BC, Wisor JP, Schmidt MA, Van Dongen HPA. Time-on-Task Effect During Sleep Deprivation in Healthy Young Adults Is Modulated by Dopamine Transporter Genotype. Sleep. 2017; 40: zsx167. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/29029252

97. Holst SC, Müller T, Valomon A, Seebauer B, Berger W, et al. Functional Polymorphisms in Dopaminergic Genes Modulate Neurobehavioral and Neurophysiological Consequences of Sleep Deprivation. Sci Rep. 2017; 7: 45982. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/28393838

98. Costa A, Riedel M, Muller U. Relationship between SLC6A3 genotype and striatal dopamine transporter availability: a meta-analysis of human single photon emission computed tomography studies. Synapse. 2011; 65: 998-1005. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21404331

99. Dauvilliers Y, Neidhart E, Lecendreux M. MAO- A and COMT polymorphisms and gene effects in narcolepsy. Mol Psychiatry. 2001; 6: 367-372. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11443519

100. Brummitt BH, Krystal AD, Siegler IC. Associations of a regulatory polymorphism of monoamine oxidase-A gene promoter (MAOA-uVNTR) with symptoms of depression and sleep quality. Psychosom Med. 2007; 69: 396-401. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17585061

101. Desautels A, Turecki G, Montplaisir J. Evidence for a genetic association between monoamine oxidase A and restless legs syndrome. Neurology. 2002; 59: 215-219. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12136060

102. Koch H, Craig I, Dahlitz M. Analysis of the monoamine oxidase genes and the Norrie disease gene locus in narcolepsy. Lancet. 1999; 353: 645-646. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10030338

103. Kozochkin DA, Manukhina EB, Downey HF. The role of microsomal oxidation in the regulation of monoamine oxidase activity in the brain and liver of rats. Gen Physiol Biophys. 2017; 36: 455-464. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/28653655

104. Wang Z, Chen L, Zhang L, Wang X. Paradoxical sleep deprivation modulates depressive-like behaviors by regulating the MAOA levels in the amygdala and hippocampus. Brain Res. 2017; 1664: 17-24. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/28365314

105. Ozen F, Yegin Z, Yavlal F, Saglam ZA, Koc H, et al. Lack of association between MAOA-uVNTR variants and excessive daytime sleepiness. Sleep Med. 2014; 15: 831-837. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23567277

106. Joëlle A. Sleep and waking in mutant mice that do not express various serotonergic transporter, monoamine oxidase A, and 5-HT1A, 5-HT1B, 5-HT2A, 5-HT2C and 5-HT7 receptors Serotonin and Sleep. Molecular, Functional and Clinical Aspects. 2008.
sleep in humans. Proc Natl Acad Sci USA. 2005; 102: 15676-15681.

108. Bachmann V, Klaus F, Bodenmann S. Functional ADA polymorphism increases sleep depth and reduces vigilant attention in humans. Cereb Cortex. 2012; 22: 962-970.

109. Radulovacki M. Role of adenosine in sleep in rats. Rev Clin Basic Pharm. 1985; 5: 327-339.

110. Mazzotti DR, Guindalini C, de Souza AA. Adenosine deaminase polymorphism affects sleep EEG spectral power in a large epidemiological sample. PLoS One. 2012; 7: e44154.

111. Mackiewicz M, Nikonova EV, Bell CC. Activity of adenosine deaminase in the sleep regulatory areas of the rat CNS. Brain Res Mol Brain Res. 2000; 80: 252-255.

112. Bachmann V, Klein C, Bodenmann S. The BDNF Val66Met polymorphism modulates sleep intensity: EEG frequency- and state-specificity. Sleep. 2012; 35: 335-344.

113. Furihata R, Saitoh K, Otsuki R. Association between reduced serum BDNF levels and insomnia with short sleep duration among female hospital nurses. Sleep Med. 2019; 68: 167-172.

114. Flores KR, Viccaro F, Aquilini M. Protective role of brain derived neurotrophic factor (BDNF) in obstructive sleep apnea syndrome (OSAS) patients. PLoS One. 2020; 15: e0227934.

115. Rahman M, Rahmani F, Rezaei N. The Brain-Derived Neurotrophic Factor: Missing Link between Sleep Deprivation, Insomnia, and Depression. Neurochem Res. 2020; 45: 221-231.

116. Cullen T, Thomas G, Wadley AJ. Sleep Deprivation: Cytokine and Neuroendocrine Effects on Perception of Effort. Med Sci Sports Exerc. 2019; 51: 1815-1825.

117. Tchekalarova J, Kortenska L, Ivanova N, Atanasova M, Marinov P. Oscillation of Hippocampal-Infralimbic proBDNF. eNeuro. 2019; 6: e29283.

118. Goel N, Banks S, Lin L. Catechol-O-methyltransferase Val158Met polymorphism associates with individual differences in sleep physiology responses to chronic sleep loss. PLoS One. 2011; 6: e29283.

119. Karen S, Edith HT, Anne E. BDNF in sleep, insomnia, and sleep deprivation. Ann Neurol. 2018; 84: 347-360.

120. Bodenmann S, Hohoff C, Freitag C, Deckert J, Rétey JV, et al. Sporadic Fatal Insomnia in Europe: Phenotypic Features and Diagnostic Challenges. Ann Neurol. 2018; 84: 347-360.

121. Medori R, Montagna P, Tiritshcher HJ, LeBlanc C, Cortelli P, et al. Fatal familial insomnia: a second kindred with mutation of prion protein gene at codon 178. Neurology. 1992; 42: 669-670.

122. Staats R. Regulation of brain-derived neurotrophic factor (BDNF) during sleep apnoea treatment. Thorax. 2005; 60: 688-692.

123. Karen S, Edith HT, Anne E. BDNF in sleep, insomnia, and sleep deprivation. Annals of Medicine. 2016; 48: 42-51.

124. Duncan WC, Sarasso S, Ferrarelli F. Concomitant BDNF and sleep slow wave changes indicate ketamine-induced plasticity in major depressive disorder. Int J Neuropsychopharmacol. 2013; 16: 301-311.

125. Dromer F, Montagna P, Tiritshcher HJ, LeBlanc C, Cortelli P, et al. Fatal familial insomnia: a second kindred with mutation of prion protein gene at codon 178. Neurology. 1992; 42: 669-670.

126. Monari L, Chen S, Brown P, Parchi P, Petersen RB, et al. Fatal familial insomnia and familial Creutzfeldt–Jakob disease: different prion proteins determined by a DNA polymorphism. Proc Natl Acad Sci U S A. 1994; 91: 2839-2842.

127. da Luz MHM, Pino JMV, Santos TG, Antunes HKM, Martins VR, et al. Sleep deprivation regulates availability of PrPc and Aβ peptides which can impair interaction between PrPc and laminin and neuronal plasticity. J Neurochem. 2020; e14960.

128. Abu-Rumeileh S, Redaelli V, Baiardi S, Mackenzie G, Windl O, et al. Sporadic Fatal Insomnia in Europe: Phenotypic Features and Diagnostic Challenges. Ann Neurol. 2018; 84: 347-360.

129. Bodenmann S, Hohoff C, Freitag C, Deckert J, Rétey JV, et al. Polymorphisms of ADORA2A modulate psychomotor vigilance and the effects of caffeine on neurobehavioural performance and sleep EEG after sleep deprivation. Br J Pharmacol. 2012; 165: 1904-1913.

130. Goldfarb LG, Petersen RB, Tabaton M, Brown P, LeBlanc AC, et al. Fatal familial insomnia and familial Creutzfeldt–Jakob disease: disease phenotype determined by a DNA polymorphism. Science. 1992; 258: 806-808.

131. Bodenmann S, Hohoff C, Freitag C, Deckert J, Rétey JV, et al. Polymorphisms of ADORA2A modulate psychomotor vigilance and the effects of caffeine on neurobehavioural performance and sleep EEG after sleep deprivation. Br J Pharmacol. 2012; 165: 1904-1913.

132. Bodenmann S, Xu S, Luhmann UF, Arand M, Berger W, et al. Pharmacogenetics of modafinil after sleep loss: catechol-O-methyltransferase genotype modulates waking functions but not recovery sleep. Clin Pharmacol Ther. 2007; 81: 692-698.

133. Bodenmann S, Xu S, Luhmann UF, Arand M, Berger W, et al. Pharmacogenetics of modafinil after sleep loss: catechol-O-methyltransferase genotype modulates waking functions but not recovery sleep. Clin Pharmacol Ther. 2007; 81: 692-698.

134. Bodenmann S, Lantford HP. Effects of modafinil on the sleep EEG depend on Val158Met genotype of COMT. Sleep. 2010; 33: 1027-1035.

135. Goel N, Banks S, Lin L. Catechol-O-methyltransferase Val158Met polymorphism associates with individual differences in sleep physiologic responses to chronic sleep loss. PLoS One. 2011; 6: e29283.

136. Wieczorek S, Gencik M, Rujescu D, Tonn P, Giegling I, et al. TNFA

https://doi.org/10.29328/journal.jnnd.1001029
promoter polymorphisms and narcolepsy. Tissue Antigens. 2003; 61: 437-442. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12823767

137. Hohjoh H, Nakayama T, Ohashi J. Significant association of a single nucleotide polymorphism in the tumor necrosis factor-alpha (TNF-alpha) gene promoter with human narcolepsy. Tissue Antigens. 1999; 54: 138-145. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10488740

138. Archer SN, Carpen JD, Gibson M, Lim GH, Johnston JD, et al. Polymorphism in the PER3 promoter associates with diurnal preference and delayed sleep phase disorder. Sleep. 2010; 33: 695-701. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20469812

139. Archer SN, Robilliard DL, Skene DJ, Smits M, Williams A, et al. A length polymorphism in the circadian clock gene Per3 is linked to delayed sleep phase syndrome and extreme diurnal preference. Sleep. 2003; 26: 413-415. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12841365

140. Ebisawa T, Uchiyama M, Kajimura N, Mishima K, Kamei Y, et al. Association of structural polymorphisms in the human period3 gene with delayed sleep phase syndrome. EMBO Rep. 2001; 2: 342-346. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11306557

141. Goel N, Banks S, Mignot E, Dinges DF. PER3 polymorphism predicts cumulative sleep homeostatic but not neurobehavioral changes to chronic partial sleep deprivation. PLoS One. 2009; 4: e8574. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19516903

142. Groeger JA, Viola AU, Lo JC. Early morning executive functioning during sleep deprivation is compromised by a PERIOD3 polymorphism. Sleep. 2008; 31: 1159-1167. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18714788

143. Viola AU, Archer SN, James LM, Groeger JA, Lo JC. PER3 polymorphism predicts sleep structure and waking performance. Curr Biol. 2007; 17: 613-618. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17346965

144. Hohjoh H, Terada N, Kawashima M, Honda Y, Tokunaga K. Significant association of the tumor necrosis factor receptor 2 (TNFR2) gene with human narcolepsy. Tissue Antigens. 2000; 56: 446-448. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11144293

145. Chen YH, Huang YS, Chen CH. Increased plasma level of tumor necrosis factor-alpha (TNF-α) gene promoter with human narcolepsy. Tissue Antigens. 2000; 54: 138-145. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10488740

146. Peyron C, Faraco J, Rogers W, Ripley B, Overeem S, et al. A mutation in a case of early onset narcolepsy and a generalized absence of hypocretin peptides in human narcoleptic brains. Nat Med. 2000; 6: 613-618. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10973318

147. Latorre D, Callweit U, Armentani E, Foglierini M1, Mele F, et al. T cells in patients with narcolepsy target self-antigens of hypocretin neurons. Nature. 2018; 562: 63-68. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/30232458

148. Takenoshita S, Sakai N, Chiba Y, Matsumura M, Yamaguchi M, et al. An overview of hypocretin based therapy in narcolepsy. Expert Opin Investig Drugs. 2018; 27: 389-406. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/29623725

149. Buhr A, Bianchi MT, Baur R. Functional characterization of the new human GABA A receptor mutation β3 (R192H). Hum Genet. 2002; 111: 154-160. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12189488

150. Wu Y, Liu HB, Ding M, Liu JN, Zhu XF, et al. Association between the -1438G/A and T102C polymorphisms of 5-HT2A receptor gene and obstructive sleep apnea and hypopnea syndrome: a systematic review and meta-analysis. Gene. 2013; 530: 287-294. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23988500

151. Wu Y, Liu HB, Ding M, Liu JN, Zhu XF, et al. Association between the -1438G/A and T102C polymorphisms of 5-HT2A receptor gene and obstructive sleep apnea and hypopnea syndrome: a systematic review and meta-analysis. Mol Biol Rep. 2013; 40: 6223-6231. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24065538

152. Van Dalfsen JH, Markus CR. The serotonin transporter gene-linked polymorphic region (5-HTTLPR) and the sleep-promoting effects of tryptophan: A randomized placebo-controlled crossover study. J Psychopharmacol. 2019; 33: 948-954. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/31237183

153. Sajadi M, Feizizadeh M, Samadi M, Foudi M, Mojiri M, et al. Stress and 5-HT2A Receptor Polymorphisms on Self-Reported Sleep Quality in Physicians in Urmq (Xinjiang, China): A Cross-Sectional Study. Int J Environ Res Public Health. 2018; 15: 1034. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/29883419

154. Zhao Y, Tao L, Nie P, Lu X, Xu X, et al. Association between 5-HT2A receptor polymorphisms and risk of obstructive sleep apnea and hypopnea syndrome: a systematic review and meta- analysis. Sleep. 2013; 530: 287-294. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23988500

155. Wu Y, Liu HB, Ding M, Liu JN, Zhu XF, et al. Association between the -1438G/A and T102C polymorphisms of 5-HT2A receptor gene and obstructive sleep apnea: a meta- analysis. Mol Biol Rep. 2013; 40: 6223-6231. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24065538

156. Van Dalfsen JH, Markus CR. The serotonin transporter gene-linked polymorphic region (5-HTTLPR) and the sleep-promoting effects of tryptophan: A randomized placebo-controlled crossover study. J Psychopharmacol. 2019; 33: 948-954. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/31237183

157. Barclay NL, Eley TC, Mill J. Sleep quality and diurnal preference in a sample of young adults: associations with SHTTLPR, PER3, and CLOCK 3111. Am J Med Genet B Neuropsychiatr Genet. 2011; 156: 681-690. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21714069

158. Brummett BH, Krystal AD, Ashley-Koch A, Kuhn CM, Züchner S, et al. Sleep quality varies as a function of 5-HTTLPR genotype and stress. Psychosom Med. 2007; 69: 621-624. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17766685

159. Carskadon MA, Sharkey KM, Knopik VS, McGeary JE. Short sleep as an environmental exposure: a preliminary study associating 5-HTTLPR interaction. PLoS One. 2018; 13: e0203137. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/29883419

160. Deuschle M, Schredl M, Schilling C, Wüst S, Frank J, et al. Association between a serotonin transporter length polymorphism and primary insomnia. Sleep. 2010; 33: 343-347. PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20337192

https://doi.org/10.29328/journal.jnnd.1001029
https://www.heighpubs.org/jnnd
023