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Reduction of REM sleep latency associated with HLA-DQB1*0602 in normal adults

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Genetic factors involved in sleep and its disorders are only starting to be isolated.¹ A relevant model is the neurological disorder narcolepsy. Narcolepsy is characterised by sleepiness, very short REM latency, and symptoms of abnormal REM sleep. It affects 0.05% of the general population in Europe and the USA. The disorder is frequently familial and strongly associated with HLA DR2 and DQB1*0602. These alleles are almost always found in narcoleptic patients but also occur in 25% of the normal population.¹ In 1986, a report by Schultz in this journal² found a reduced REM sleep latency in DR2-positive normal volunteers, a result they were not able to replicate in a second sample.³ We retested this hypothesis in a large population-based sample of polygraphically recorded adults.⁴

The sample included 509 normal adults enrolled in the Wisconsin Sleep Cohort Study⁴ (209 women and 280 men, 50 [8] years of age; 98% white). Informed consent was obtained for all volunteers. The presence or absence of DQB1*0602 was determined with established sequence specific primer and oligotyping techniques. Polysomnographic variables (table) were then compared by DQB1*0602 status by linear regression analysis with adjustment for possible confounding factors including sex, age, body-mass index, amount of sleep the night before polysomnography, and severity of sleep apnoea (apnoea hypopnoea index).

A highly statistically significant 18 min reduction in REM latency was observed in DQB1*0602 positive volunteers. This effect was associated with an increase in percent REM sleep and with changes indicative of greater sleep continuity, such as less stage one, less percent wake after sleep onset, and better sleep efficiency. This finding demonstrates for the first time with a large sample and proper control of confounding factors that the genetic background at the level of HLA influences normal sleep, with special emphasis on REM sleep. Notably, the difference in REM latency obtained in our sample was similar to that estimated when both Schultz samples were combined (101 [7] min, n=39 vs 121 [7] min, n=63, for positive and negative, respectively, p=0.05).

Narcolepsy is well known to be associated with abnormal REM tendencies. Our result could thus be explained by unsuspected narcolepsy phenotypes with very short REM

Sleep variable	DQB1*0602 positive (n=127)	DQB1*0602 negative (n=363)	p
Time in bed (min)	440 (4)	445 (3)	0.38
Total sleep time (min)	383 (5)	378 (3)	0.40
Sleep efficiency (%)	87.1 (0.8)	85.0 (0.5)	0.03
Sleep onset latency (min)	8.5 (1.2)	10.9 (0.7)	0.11
REM sleep latency (min)	104 (6)	122 (3)	0.008
% wake after sleep onset	13.5 (1.1)	16.0 (0.7)	0.06
% stage 1	7.8 (0.4)	9.2 (0.3)	0.007
% stage 2	56.8 (0.9)	56.3 (0.5)	0.66
% stage 3	12.1 (0.6)	12.2 (0.3)	0.91
% stage 4	4.2 (0.5)	4.5 (0.3)	0.69
% REM sleep	19.0 (0.6)	17.7 (0.3)	0.05

Data are means (SE) adjusted for age, sex, body-mass index, apnoea-hypopnoea index, and amount of sleep the night before nocturnal polysomnography.

Sleep variables in DQB1*0602 positive and negative volunteers

latencies in the DQB1*0602 positive group. However, less than one narcoleptic patient would be expected in this sample based on prevalence data. Furthermore, a comparison of the distribution of REM sleep latencies in both groups did not substantiate this hypothesis; there was no evidence for bimodality in the DQB1*0602 positive group (data not shown). Rather, the data suggest a direct effect of the DQB1*0602 genotype that results in a shifted distribution. HLA DQ might thus be the first genetic factor identified that influences normal sleep patterns in the general population.

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How to detect visual neglect in acute stroke

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Visual neglect can be a major disability after stroke and may impede rehabilitation.^{1,2} Early detection of the disorder is important for allocation of rehabilitation resources.³ We studied to what extent visual neglect can be measured as a solitary defect and how it can be assessed in acute stroke patients.

A consecutive series of 52 patients with a first-ever single acute right hemisphere brain infarct admitted to Tampere University Hospital was assessed for visual neglect by the six conventional subtests of the behavioural inattention test⁴ (BIT) within 10 (mean 6.0 [SD 2.0]) days of stroke. The lesions were visualised with computed tomography or magnetic resonance imaging. The exclusion criteria were history of neurological disorders, premorbid cognitive deterioration, insufficient cooperation, primary visual impairment, left-handedness, and age over 75 years. The mean age was 63 (10) years and the mean number of years