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HLA-DR2 and Sleep Onset REM Periods in Depression

To the Editor:

Virtually all patients with narcolepsy/cataplexy are HLA-DR2 positive, in contrast to an approximately 25% incidence of this human leukocyte antigen (HLA) in the general population (cf. Honda and Juji 1988). Given the close association between narcolepsy and HLA-DR2 on the one hand, and the most typical sleep alteration, i.e., sleep onset rapid eye movement (REM) periods (SOREMPs) in narcoleptic patients on the other (Vogel 1960), the question arises as to whether there is a direct link between DR2 and certain features of sleep structure. The aim of the present study was, therefore, to look for HLA-DR2 incidence in depression, an illness that shares—even though less regularly—the feature of shortened REM latency with narcolepsy (Coble et al 1981).

Recently Montplaisir et al (1990) failed to show an increased occurrence of HLA-DR2 in unipolar depression, as against Riemann et al. (1988), who in a pilot study, reported 4 of 7 patients with a major depressive disorder and at least one SOREMP during night sleep to be HLA-DR2 positive. A possible explanation for these conflicting results could be a depression-independent impact of HLA-DR2 on sleep structure. We, therefore, examined the frequency of HLA-DR2 in a larger sample of depressed patients, restricting our post hoc examination to those depressives who displayed SOREMPs in standard night polysomnography and, thereby, share this typical sleep alteration with narcoleptics.

Sixteen patients (8 men and 8 women) with a major depressive disorder/endogenous subtype (Research Diagnostic Criteria, RDC) (Spitzer et al 1978) were investigated, all giving informed consent. The mean age (± SD) was 47.3 ± 7.5 years. Thirteen of the patients under investigation displayed a SOREMP (REM sleep latency after first epoch S2 sleep <15 min) at least once during night sleep recordings, whereas the other 3 patients exhibited REM latencies of 18, 21, and 23 min.

On the average, one or two nights of baseline sleep were recorded for each patient, applying standard night somnopolygraphy (EEG, EMG, EOG). Patients were free of any psychoactive medication at least 1 week prior to sleep recordings; urinary drug monitoring was carried out regularly. Sleep recordings and analysis were carried out according to the guidelines proposed by Rechtschaffen and Kales (1968). The following sleep parameters were determined: sleep period time (SPT); sleep onset latency (min, defined as first epoch S2 sleep); REM sleep latency (min, defined as the time interval between sleep onset and REM start); sleep efficiency (%); and the percentages for REM and slow wave sleep (S3 + S4), both based on SPT. HLA-typing was determined by duplicate serological testing and by restriction fragment length polymorphism (RFLP) analysis (cf. Geisler and Albert 1989).

Concerning our target variable, mean REM latency (± SD) was 10.6 ± 6.4 min. Analysis of the other sleep parameters revealed a low sleep efficiency (72.1% ± 20.1%), a rather long sleep onset latency (27.8 min ± 18.5 min), a normal amount of REM sleep (23.6% ± 9.7%), and a low percentage of slow-wave sleep (6.8 ± 6.7% SPT). HLA typing revealed an incidence of HLA-DR2 of 25% (or 4 of 16 patients under investigation).

In our subgroup of depressed patients, showing at least one SOREMP during polygraphic sleep re-

cording, the incidence of HLA-DR2 was only 25%. This observation strongly underlines the findings of Montplaisir et al (1990) that the frequency of HLA-DR2 in depressed patients in general is not different from that found in normal controls. Furthermore, our results clearly refute the assumption of a direct immunogenetic association between abbreviated REM-sleep latency (including SOREMPs) and HLA-DR2. Finally, the present results are in agreement with previous findings showing that REM latency in normal subjects does not correlate with the HLA-DR2 haplotype (Schulz et al 1987).

From this evidence we conclude that the presence of HLA-DR2 and an increased propensity toward SOREMPs are two independent features. This suggests that HLA-DR2 may be instead associated with cataplexy, a pathophysiological event that is peculiar to narcolepsy (Guilleminault 1976), and that has never been reported for depressives or other subjects with shortened REM latency.

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