

Observations

Multiple sclerosis and Type I diabetes

To the Editor: Multiple sclerosis (MS) and Type I diabetes mellitus are both believed to result from interaction between genetic and environmental factors. The incidence of these diseases varies from country to country, and marked differences can also be observed between ethnically distinct groups within a country.

For instance, the incidence of Type I diabetes on the island of Sardinia is four to five times higher than that of continental Italy [1], and similar figures have been reported for multiple sclerosis. Sardinia and continental Central Italy are 200 km apart with residing populations exposed to similar environmental factors. This suggests that the differences in the incidence of Type I diabetes and multiple sclerosis are primarily a result of genetic rather than environmental factors. This conclusion is supported (at least for T1DM) by the observation that, among the children of Sardinian parents who have migrated into the Lazio region of continental Italy, the high incidence of this disease that characterizes their ancestral population has been retained [2].

Marrosu et al. [3] have reported an increased prevalence of Type I diabetes in a cohort of Sardinians with multiple sclerosis. They suggested that susceptibility to both of these autoimmune diseases might be conferred by the same HLA haplotype. As they noted, previous studies have shown that multiple sclerosis in Sardinia is most strongly associated with two HLA DR-DQ haplotypes, DRB1*0301-DQA1*0501-DQB1*0201 and DRB1*0405-DQA1*0501-DQB1*0301, the first of which is known to bestow high susceptibility to Type I diabetes. In contrast, in northern European populations, multiple sclerosis shows a stronger relation with the DR15 haplotype, which confers dominant protection against Type I diabetes.

In the Lazio region of Italy, there is no multiple sclerosis patient registry and no published data on multiple sclerosis patients of Sardinian origin in this area. However, the Eurodiab Registry for Type I diabetes, which was established in 1989

Table 1. Phenotypic distribution of HLA DRB1 in Continental Italians with Type I diabetes or multiple sclerosis and control subjects

HLA	Type I diabetes mellitus <i>n</i> =490 (%)	Multiple sclerosis <i>n</i> =315 (%)	Control subjects <i>n</i> =718 (%)
DR3	277 (57) ^a	62 (20)	126 (18)
DR4	269 (55) ^b	59 (19)	113 (16)
DR15	17 (3.5) ^a	98 (31) ^d	83 (12)

^a χ^2 test Type I diabetes vs control subjects, $p < 10^{-4}$, OR 6.1 (CI 5–8)

^b χ^2 test Type I diabetes vs control subjects, $p < 10^{-4}$, OR 6.5 (CI 5–8.5)

^c χ^2 test Type I diabetes vs controls subjects, $p < 10^{-4}$, OR 0.3 (CI 0.16–0.5)

^d χ^2 test multiple sclerosis vs control subjects, $p < 10^{-4}$, OR 3.5 (CI 2.5–5)

[4], currently includes over 900 cases from the Lazio region, and none of these patients has multiple sclerosis. We, therefore, analysed the HLA class II typing data for 450 of these Type I diabetes patients, 315 patients with multiple sclerosis (unpublished data), and 719 control subjects, all residents of continental Italy. As shown in Table 1, the Type I diabetes susceptibility haplotypes DR3 and DR4 are not associated with multiple sclerosis in our cohort. Susceptibility to the latter disease seems to depend more on having the DR15 haplotype, which is, as reported [5], infrequent among Type I diabetic patients.

This finding can explain why the two diseases are not associated in continental Italy, which is highly similar to Sardinia in terms of environment and lifestyle. The common predisposition to both multiple sclerosis and Type I diabetes suggested by the data of Marrosu et al. seems to have a primarily genetic basis that could be unique to the Sardinian population.

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