

Table 1. Demographic and clinical variables of subjects

	Controls	MS patients				
		Total group	RR	SP	PP	CIS*
number of subjects	300	307	229	34	20	24
Gender (M:F)	115:185	109:198	80:149	10:24	11:9	8:16
Age, yrs	38.6±0.9	48.6±0.9	38.7±0.8	59.6±1.2	47.5±2.8	34.0±1.7
Age at onset, yrs		31.7±0.6	30.7±0.7	32.1±1.8	39.4±3.1	33.2±1.9
Disease duration, yrs		8.3±0.5	7.1±0.5	19.7±1.9	11.7±2.0	1.3±0.2
Time to SP conversion, yrs				10.9±1.3		
Time between the first and the second attack, yrs			3.2±0.4 (n=135)^			
Annual relapse rate <sup>°</sup>			1.0±0.1 (n=91)^			
EDSS		2.4±0.1 (n=274)^	1.8±0.1 (n=206)^	5.8±0.2 (n=27)^	5.9±0.4 (n=18)^	1.3±0.1 (n=22)^
Progression Index <sup>°</sup>		0.42±0.04 (n=194)^	0.32±0.03 (n=142)^	0.52±0.09 (n=27)^	0.89±0.16 (n=18)^	
Ranked severity score <sup>°</sup>		0.26±0.02 (n=88)^	0.20±0.01 (n=65)^	0.33±0.04 (n=23)^	0.60±0.09 (n=14)^	

Data are given as means ± S.E.M.; EDSS= Expanded Disability Status Scale; progression index =EDSS /disease duration (yrs); annual relapse rate=total amount of relapses/duration of disease (≥2 yrs)

\* Clinical Isolated Syndrome suggestive of MS with dissemination of lesions in time and in space at MRI, according to McDonald.

<sup>°</sup> calculated before any immunomodulatory treatment

<sup>^</sup> patient numbers available for respective analysis

Table 2. *G98T* allele and genotype frequencies (%) in MS patients and healthy controls

<i>G98T</i> frequencies	Controls	All MS	MS Subtypes			
	n=300	n=307	RR-MS n=229	SP-MS n=34	PP-MS n=20	CIS n=24
Allele						
<i>G</i>	517 (86.2)	508 (82.7)	373 (81.4)	60 (88.2)	35 (87.5)	40 (83.3)
<i>T</i>	83 (13.8)	106 (17.3)	85 (18.6)	8 (11.8)	5 (12.5)	8 (16.7)
Genotype						
<i>G/G</i>	220 (73.3)	215 (70.0)	156 (68.2)	27 (79.4)	15 (75)	17 (70.8)
<i>G/T</i>	77 (25.7)	78 (25.3)	61 (26.6)	6 (17.7)	5 (25)	6 (25)
<i>T/T</i>	3 (1.0)	14 (4.7)*	12 (5.2) <sup>°</sup>	1 (2.9)	0 (0)	1 (4.2)

Values are expressed as n (%)

\**P*= 0.01 for all MS patients vs healthy controls; OR(95%CI): 4.7 (1.3-16.6)

<sup>°</sup>*P*= 0.006 for RR-MS patients vs healthy controls; OR(95%CI): 5.5 (1.5-19.6)

Table 3. *A516C* allele and genotype frequencies (%) in MS patients and healthy controls

<i>A516C</i> frequencies	Controls	All MS	MS Subtypes			
	n=300	n=307	RR-MS n=229	SP-MS n=34	PP-MS n=20	CIS n=24
Allele						
<i>A</i>	522 (87.0)	528 (86.0)	392 (85.6)	62 (91.2)	34 (85.0)	40 (83.3)
<i>C</i>	78 (13.0)	86 (14.0)	66 (14.4)	6 (8.8)	6 (15.0)	8 (16.7)
Genotype						
<i>A/A</i>	225 (75.0)	227 (74.0)	167 (73.0)	29 (85.3)	15 (75.0)	16 (66.7)
<i>A/C</i>	72 (24.0)	74 (24.0)	58 (25.3)	4 (11.8)	4 (20.0)	8 (33.3)
<i>C/C</i>	3 (1.0)	6 (2.0)	4 (1.7)	1 (2.9)	1 (5.0)	0 (0)

Values are expressed as n (%)

Table 4 . *G98T* and *A516C* allele and genotype frequencies (%) in RR-MS patients with a duration of the disease of 10 years or more, classified as “benign” if EDSS was lesser than 2 (according to Pittock et al.)

	RR-MS ≥ 10 yrs benign n=29	RR-MS ≥ 10 yrs n=27		RR-MS ≥ 10 yrs benign n=29	RR-MS ≥ 10 yrs n=27
<i>G98T</i> frequencies			<i>A516C</i> frequencies		
Allele			Allele		
<i>G</i>	49 (84.5)	39 (72.3)	<i>A</i>	51 (88.0)	45 (83.3)
<i>T</i>	9 (15.5)	10.5 (27.7)	<i>C</i>	7 (12.0)	9 (16.7)
Genotype			Genotype		
<i>G/G</i>	20 (69.0)	15 (55.6)	<i>A/A</i>	24 (82.8)	18 (66.6)
<i>G/T</i>	9 (31.0)	9 (33.3)	<i>A/C</i>	3 (10.3)	9 (33.3)
<i>T/T</i>	0 (0)	3 (11.1)	<i>C/C</i>	2 (6.9)	0 (0)

Values are expressed as n (%)

Table 5 . *G98T* and *A516C* allele and genotype frequencies (%) in SP-MS compared with RR-MS patients with a duration of the disease longer than 10 years

	SP-MS n=34	RR-MS > 10 yrs n=59		SP-MS n=34	RR-MS > 10 yrs n=59
<i>G98T</i> frequencies			<i>A516C</i> frequencies		
Allele			Allele		
<i>G</i>	60 (88.3)	94 (79.7)	<i>A</i>	62 (91.2)	100 (84.8)
<i>T</i>	8 (11.7)	24 (20.3)	<i>C</i>	6 (8.8)	18 (15.2)
Genotype			Genotype		
<i>G/G</i>	27 (79.4)	38 (64.4)	<i>A/A</i>	29 (85.3)	44 (74.6)
<i>G/T</i>	6 (17.6)	18 (30.5)	<i>A/C</i>	4 (11.8)	12 (20.3)
<i>T/T</i>	1 (3.0)	3 (5.1)	<i>C/C</i>	1 (2.9)	3 (5.1)

Values are expressed as n (%)

Table 6 . Haplotypes distribution in MS patients compared with controls

Haplotypes	MS patients n = 307	Controls n = 300
<i>GG/AA</i>	197 (64.2)	209 (69.7)
<i>GT/AA</i>	25 (8.1)	16 (5.3)
<i>TT/AA</i>	5 (1.6)	0 (0)
<i>GG/AC</i>	14 (4.6)	12 (4)
<i>GT/AC</i>	51 (16.6)	59 (19.7)
<i>TT/AC</i>	9 (2.9)	1 (0.3)
<i>GG/CC</i>	4 (1.3)	0 (0)
<i>GT/CC</i>	2 (0.7)	1 (0.3)
<i>TT/CC</i>	0 (0)	2 (0.7)

Values are expressed as n (%)

Table 7. Demographic and clinical variables of RR-MS patients stratified by the presence of *T* or *C* mutated alleles, or both

	<b>RR-MS patients</b>	<i>T-/C-</i>	<i>T+/C-</i>	<i>T-/C+</i>	<i>T+/C+</i>	
Disease duration, yrs	7.1±0.5	7.9±0.6	11.4±2.0	8.4±1.9	8.2±1.2	
Age at onset, yrs	30.7±0.7	32.1±0.8	31.1±1.6	29±2.3	27.3±1.6	
Time between the first and the second attack, yrs	3.2±0.4	3.9±0.6	4.3±1.1	1.7±0.6	2.8±0.6	
Annual relapse rate <sup>°</sup>	1.0±0.1	1.18±0.15	0.74±0.21	1.34±0.33	0.89±0.17	
Progression Index <sup>°</sup>	0.32±0.03 (n=142) <sup>^</sup>	0.37±0.05	0.16±0.02	0.29±0.08	0.42±0.10	
Ranked severity score <sup>°</sup>	0.20±0.01 (n=65) <sup>^</sup>	0.23±0.02	0.14±0.04	0.17±0.05	0.18±0.02	Data are given as means ± S.E.M.;

Progression Index = Expanded Disability Status Scale /disease duration (yrs);

annual relapse rate=total amount of relapses/duration of disease (≥2 yrs)

<sup>°</sup> calculated before any immunomodulatory treatment

<sup>^</sup> patient numbers available for respective analysis