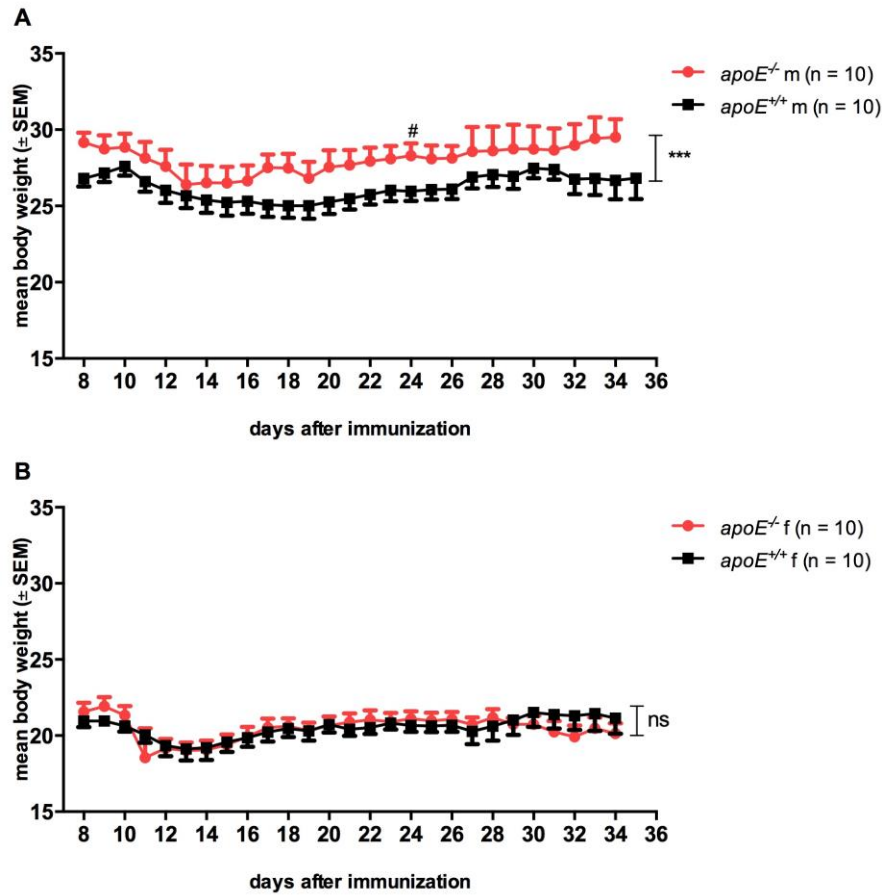
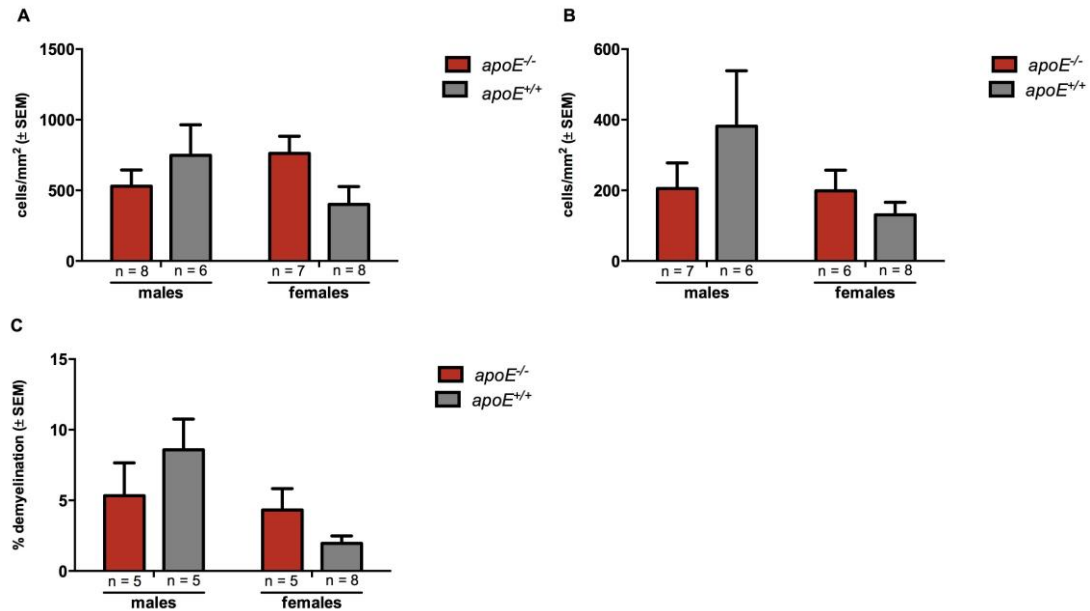


Supplementary Figure 1: Body weight of C57Bl/6 wildtype ($apoE^{+/+}$) and $apoE$ -deficient ($apoE^{-/-}$) mice during active MOG₃₅₋₅₅ EAE.



Legend: The graphs show the mean body weight of mice during MOG₃₅₋₅₅ induced EAE. (A) Body weight of male (m) $apoE^{-/-}$ mice was higher than of $apoE^{+/+}$ mice (cumulative mean weight: male $apoE^{+/+}$ = 26.2 ± 0.8 g, n = 10, male $apoE^{-/-}$ = 28.1 ± 0.9 g; n = 10; p < 0.001); (B) In females, body weight was nearly the same in both genotypes (cumulative mean weight: female $apoE^{+/+}$ = 20.5 ± 0.7 g, n = 10, female $apoE^{-/-}$ = 20.5 ± 0.8 g; n = 10; p = 0.8).

Supplementary Figure 2: Histopathological assessment after active MOG₃₅₋₅₅ EAE.



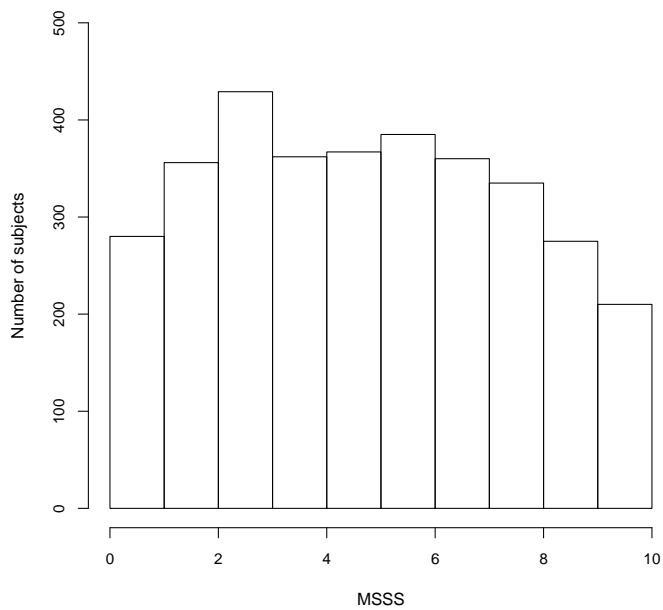
Legend: Quantification of Mac3⁺ cells (macrophages, A); CD3⁺ cells (T cells, B) and demyelinated area (FluoromyelinTMRed, C) in the lumbar spinal cord of female and male wildtype (*apoE*^{+/+}) and *apoE*-deficient (*apoE*^{-/-}) mice 26 and 35 days after immunization (pooled from both independent EAE-experiments, see manuscript fig. 1A, 1B). Statistical analyses: unpaired t-test yielding no significant differences.

Supplementary Table 1: Demographic details of all included patients.

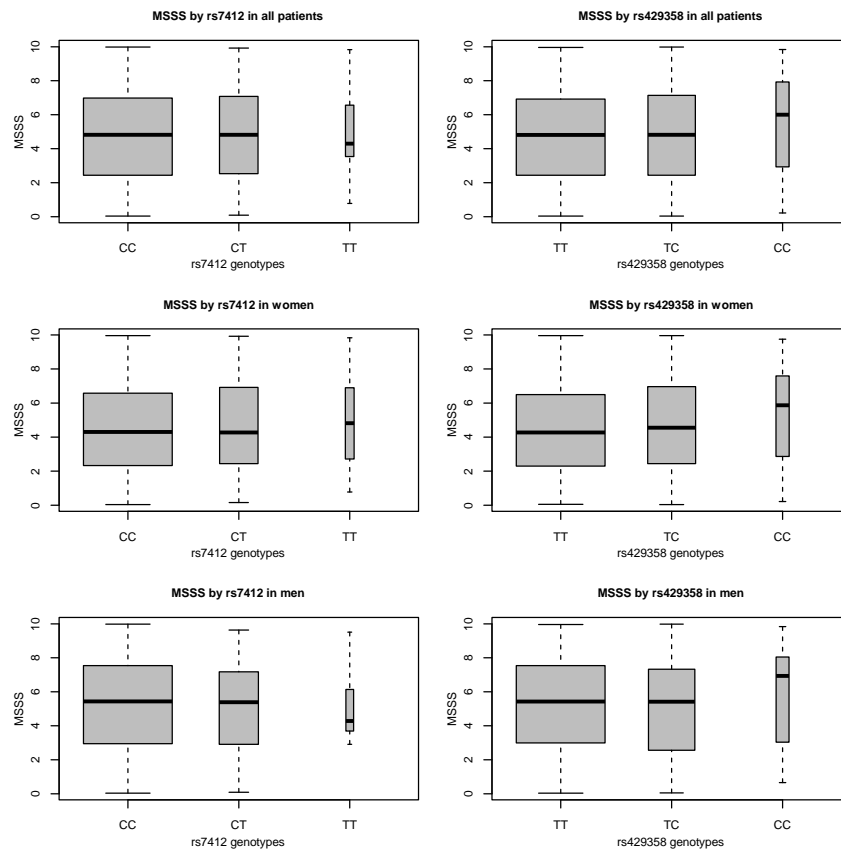
Center	N cases (% women)	Age at onset (median, IQR)	MSSS (median, IQR)	MAF rs7412 rs429358
Bochum	688 (70.5)	30 (24-38)	5.15 (2.97-7.33)	0.0932 0.1368
Mainz	149 (62.4)	33 (27-41)	6.14 (3.69-7.83)	0.1081 0.1443
Munich	409 (73.3)	28 (22-36)	4.35 (2.44-6.46)	0.0860 0.1127
Paris	1,044 (71.0)	32 (25-39)	4.55 (2.10-6.81)	0.0768 0.1272
Rostock	469 (72.3)	31 (24-39)	3.65 (1.77-6.46)	0.0906 0.1239
Wuerzburg	478 (69.5)	27 (21-34)	4.93 (2.87-6.94)	0.0895 0.1250
Total	3,237 (70.8)	30 (24-38)	4.81 (2.44-6.94)	0.0867 0.1274

Legend: N = number, IQR = interquartile range, MAF = minor allele frequency
(corresponding to the T allele of rs7412 and the C allele of rs429358).

**Supplementary Figure 3: Distribution of the MS Severity Score in 3,237
German and French patients.**



Supplementary Figure 4: Distribution of the MS Severity Score by rs7412 and rs429358 genotypes in all patients and after sex stratification.



Legend: The box plot shows the distribution of the MS Severity Score (MSSS) dependent on the rs7412 and rs429358 genotypes. Horizontal lines represent median values, boxes represent interquartile ranges, and whiskers extend to 1.5× the interquartile range. Box sizes are scaled to represent the underlying sample size.