

# Glutathione S-transferase polymorphisms in MS

## Their relationship to disability

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**BACKGROUND:** Oxidative stress has been implicated in inflammatory demyelination. The glutathione S-transferase (GST) supergene family encodes isoenzymes that appear to be critical in protection against oxidative stress. Certain GST loci are polymorphic, demonstrating alleles that are null (GSTM1/GSTT1), encode low activity variants (GSTP1), or are associated with variable inducibility (GSTM3).

**OBJECTIVES:** To investigate the association between clinical outcome in MS and allelic variants of GSTM1, GSTM3, GSTT1, and GSTP1.

**METHODS:** Four hundred patients with clinically definite MS were studied. Disability was measured using the Kurtzke Expanded Disability Status Scale (EDSS). Disability was graded as mild (EDSS 0–4), moderate (4.5–5.5), or severe (EDSS 6–10). PCR-based genotyping was performed using DNA extracted from lymphocytes. Significant associations between GST genotypes and clinical outcome were corrected for gender, onset age, and disease duration using logistic regression.

**RESULTS:** We found that the GSTM3 AA genotype was associated with severe disability in patients with a disease duration of more than 10 years ( $p = 0.027$ ,  $n = 177$ , OR = 2.4, 95% CI = 1.1–5.0). Homozygosity for both *GSTM1\*0* and *GSTP1\*Ile<sup>105</sup>* containing allele was associated with severe disability in patients with a disease duration greater than 10 years ( $p = 0.022$ ,  $n = 179$ , OR = 5.0, 95% CI = 1.3–19.8).

**CONCLUSIONS:** Our results suggest that long-term prognosis in MS is influenced by a genetically determined ability to remove the toxic products of oxidative stress.

