Table 1 Individual marker analysis for association with multiple sclerosis susceptibility

	Location	MAF	p*	P _{corr} †
rs928736	–2561	0.306	0.84	–
Ser repeat	230	0.048	0.80	–
707C/T	707	0.066	0.72	–
840C/A	840	0.001	–	–
rs11554599	1311	0.065	0.63	–
rs11554600	1688	0.128	0.15	–
rs7278735	2633	0.180	0.022	0.11

Location relative to transcription start; MAF, minor allele frequency in 3748 independent parental chromosomes; Ser, serine.

*p Value in a TRANSMIT test (<http://www-gene.cimr.cam.ac.uk/clayton/software/>) with 10 000 bootstrap replicates; †p value after multiple testing correction according to the method suggested by Nyholt (<http://genepi.qimr.edu.au/general/daleN/SNPSPD/>), which indicates that the six analysed markers behave as five independent ones.

major myelin-specific genes during oligodendrocyte maturation in the brain,² and remyelination after injury is impaired in *Olig1*^{–/–} mice.¹ In patients with multiple sclerosis, remyelinating capacity is limited even though oligodendrocyte precursor cells are often efficiently recruited.⁴ These findings raise the question whether genetic variants in the *Olig1* gene (*Olig1*) influence remyelinating capacity and vulnerability to the consequences of a demyelinating event.⁵

To investigate this hypothesis, we first aimed at identifying any *Olig1*-coding variants by resequencing the coding region in 20 patients with multiple sclerosis having at least one affected first-degree relative. Three coding variants were identified: a (TCC)_n repeat between nucleotides 230 and 247, leading to a variable number (3–9) of serine residues starting from codon 43 in the protein sequence; a synonymous C/T single-nucleotide polymorphism (SNP) at position 707 (codon 202); and a non-synonymous C/A SNP at position 840, leading to a substitution of threonine by asparagine at codon 246. Inspection of the public databases showed a further five SNPs in the 3' untranslated region (3'UTR), but no other variant in the coding region. A robust assay could not be designed for three of these UTR SNPs.

Subsequently, we elected to investigate the novel variants, remaining 3'UTR variants, and the first SNP upstream and downstream of the gene typed in the HapMap project for association with susceptibility to multiple sclerosis. We typed these seven variants in 937 UK trio families (an affected individual and both parents). Patients satisfied Poser criteria for the diagnosis of multiple sclerosis and had typical demographic features, with a mean age of 37.8 years, mean Expanded Disability Status Scale of 4.3, mean disease duration of 11.9 years and a male:female ratio of 1:3. All participants gave written

informed consent and the study was approved by the local ethics committee. Four SNPs (707CT, 840AC, rs11554599 and rs11554600) were typed with Taqman Assays-by-Design and two (rs928736 and rs7278725) with Assays-on-Demand (Applied Biosystems). The serine repeat polymorphism was amplified in a polymerase chain reaction and fluorescently labelled fragments were separated on a 3700 capillary sequencer (Applied Biosystems, Foster City, California, USA).

No markers deviated significantly from Hardy–Weinberg equilibrium, and genotyping success rates were >98.5% for all SNPs and 91.8% for the serine repeat polymorphism. For each marker, 166 participants were typed in duplicate. No inconsistency was seen for any of the SNPs and not more than two inconsistent alleles were seen for the serine repeat microsatellite. Only two mendelian errors (one for rs11554600 and rs7278725 each) were observed. The minor allele frequency for the 840C/A coding variant was only 0.1%, thereby preventing a meaningful analysis. For the serine repeat polymorphism, alleles with a frequency of <5% were grouped together. Evidence for association was sought by transmission disequilibrium testing using the TRANSMIT program, with 10 000 bootstrap replicates used to provide an empirical estimate of statistical significance. Marker rs7278735 showed borderline nominally significant evidence for association (table 1).

The data were also analysed by using the Haploview program (<http://www.broad.mit.edu/mpg/haploview/>). All markers except rs928736 were found to lie in the same haplotype block (accepting the program's default definitions), within which five haplotypes with a frequency of ≥5% were observed. A haplotype transmission disequilibrium test on these showed overtransmission of the most frequent haplotype, but

again this trend was not significant after appropriate correction for multiple testing (table 2).

In conclusion, we have identified novel coding variants in the *Olig1* gene, including a trinucleotide repeat, but have found no evidence to support the hypothesis that genetic variation in *Olig1* influences susceptibility to multiple sclerosis.

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BOOK REVIEWS

Fast facts: multiple sclerosis

Edited by George D Perkin, Jerry S Wolinsky. Published by Health Press, Oxford, 2005, £15.00 (soft cover), pp 89. ISBN 1-903734-70-3

It would perhaps seem a tall order to compress into 89 pages the essence of a puzzling disease—cause unknown and treatment evolving—but I think the two well-known authors of *Fast facts: multiple sclerosis* have largely managed to achieve this. They have been able to carry out this task, from their lifelong experience in managing patients with multiple sclerosis and as a result they have been able to pull out and then elaborate on both the common and the difficult cases, against a backdrop that is well illustrated and fast flowing, interspersed with clinical vignettes. Some examples are as follows:

Table 2 Haplotype analysis for markers serine repeat–707C/T–rs11554599–rs11554600–rs7278735

Haplotype	Frequency	p*
6-C-C-G-C	0.705	0.021
6-C-C-A-T	0.129	0.037
6-T-T-G-C	0.065	0.65
6-C-C-G-T	0.051	0.19
X†-C-C-G-C	0.049	0.73
Global		0.072

*Uncorrected p values in a TRANSMIT test with 10 000 bootstrap replicates; †X, any alternative allele (3, 4, 7, 8 or 9 serine repeats).

- A neat table defining the familial risk of disease development from the index case
- Common questions and their pragmatic answers covering scenarios such as the effects of pregnancy, vaccination and anaesthetic on the patient
- The newly updated McDonald criteria
- The pros and cons of the different β interferons or glatiramer and the recent monoclonal antibody studies
- The vital links that need to be established and maintained between secondary and community services.

Of course, many excellent and deeply crafted works on multiple sclerosis are already in print, in addition to the hundreds of papers published each year (I found about 2000 papers on a simple PubMed search for 2005), but perhaps that is just the point about this small book. For the registrar seeing his or her first patients with the disease; for the consultant who needs answers to the tricky questions that are often asked at the end of the consultation; and even I would suggest, for patients who need a little more than access to a website as they start to ruminate on the difficult questions, in between the 6-month outpatient appointments. For all these different needs this slim volume has a role in alleviating, to some extent, the problems and worries of this unpleasant and enigmatic disease.

J Chataway

Handbook of Neurologic Rating Scales, 2nd edn.

Edited by R M Herndon. Published by Demos Medical, New York, 2006, £82.25 (hardcover), pp 434. ISBN 1-888799-92-7.

Rating scales now have an established role as primary and secondary outcome measures for clinical studies. They are also frequently used in clinical practice. Consequently, data generated by rating scales will increasingly influence patient care, prescribing and policy. Therefore, clinicians need to take their rating scales very seriously.

Herndon's book is a welcomed addition to my shelf. It has 17 chapters, 15 of which give accounts of rating scales by diagnosis (eg, multiple sclerosis, stroke), clinical problem (eg, headache, movement disorders, ataxia)

or treatment (eg, rehabilitation). Each chapter has an introduction, details about the development and evaluation of a range of rating scales and assessment methods, and a short summary.

The strong points of the book are that it brings together a large number of scales, and for each gives an overview under a series of consistent headings: validation, administration and scoring, advantages, disadvantages and summary. In doing so, it gives clinicians a compendium of scales with useful evaluations and references. In addition, a great feature is that exhibits from the book—pdf copies of scales—can be downloaded. This will save considerable time and avoid the sad situation when rating scales are typed out inaccurately (oh yes, it does happen!).

Some of the limitations of the book are obvious and are covered in Robert Herndon's preface. Firstly, this is by no means an exhaustive list of rating scales. It couldn't be—the field is changing fast, with scales being published regularly. So readers need to supplement this with other sources including, for example, the database of patient-reported outcome and quality-of-life instruments (ProQolid; www.proqolid.org). Secondly, the evaluations of the scales listed are often fairly brief, so again these may need to be supplemented by further exploration.

From my perspective, the book has another limitation. It would benefit from chapters on rating scale theory and a practical guide to scale selection. Hopefully, these will appear in the next edition. That being said, I think Robert Herndon has achieved his goal of producing a valuable text for those planning clinical trials and those wishing to have a better understanding of their meaning.

J C Hobart

Surgical and medical treatment in art

Edited by Alan E H Emery, Marcia L H Emery. Published by The Royal Society of Medicine Press, London, 2006, £45.00 (hardcover), pp 139. ISBN 1-85315-695-7.

The interface between medicine and art has always been blurred, particularly with the work of such famous men as Leonardo da Vinci, whose 15th century drawings of the human body would not be out of place in a modern-day anatomy textbook. Consequently, a book such as this, which

portrays how artists have depicted medical and surgical therapies over the centuries, will appeal to anyone who is interested in both medicine and art.

The book is presented as a series of colour plates covering a wide range of styles and techniques and spanning a period from ancient Egyptian murals to modern works based on cytogenetics. The artists include several artistically talented medics, artist patients depicting their own experiences and famous artists well known to us all. The pictures range from being realistic to those which are bizarre caricatures, and, although some are merely factual, others convey emotions, such as humour, despair, desperation and resignation. Each artwork is accompanied by a short treatise giving information on the artist and describing the relevance of the work.

This book is a companion to a previous volume *Medicine in art* by the same authors. The book is well researched and the authors' passion for medicine and art shines through. There are some high-profile omissions (eg, Hogarth's painting on Christ healing the sick at "The Pool of Bethesda"), but this is inevitable given the size of the book. Some of the works are portraits depicting famous physicians or surgeons of their time and so are only loosely related to "treatment". Each of the artworks is reproduced to a high standard, making the book aesthetically very attractive.

This is a book for dipping into rather than for daily use but, like books on medical quotations, it is definitely worth a place in the library of those whose interest in medicine goes beyond the mundane.

M Rose, P Domizio

CORRECTION

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N Arai, C Shikai, S Fuse, *et al.* Severe amnesia after a restricted lesion in the left hippocampal body (*J Neurol Neurosurg Psychiatry* 2006;**77**:1196–7). The corresponding author, Y Sakurai, should have appeared in the author list. The correct author list is: N Arai, Y Sakurai, C Shikai, S Fuse, and T Shimpo. We apologise for this error.