Discussion This is the first in vivo study in Parkinsonian subjects using a prolonged 18F-dopa PET scanning protocol to detect differences in dopamine influx constant in the functional COMT val158met polymorphism. Our results suggest that a higher Ki constant, indicative of a higher presynaptic dopamine level in the frontal regions of met homozygotes, supports clinical data on the distinct phenotypic differences as found in other studies.

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Results To date notes from 155 consecutive patients have been examined (2002–2011). There is a thyroid disturbance in 34.1%, in 5.2% the disturbance being only immunological (TPO positive), while 28.9% have a biochemical and/or clinical thyroid disturbance. Of these last group there have been 19 thyrotoxicosis cases (14.1%) with an onset date between 14 and 45 months after the 1st Campath dose, 1 thyroid eye disease (0.7%), eight transient hyperthyroidism (5.9%) and 13 hypothyroidism (9.6%). All the patients with thyrotoxicosis received Carbimazole and two radioiodine. Of note from the 25 TPO positive patients only seven haven’t developed a biochemical or clinical thyroid complication.

Conclusion Campath induced thyroid disturbance in MS appears common and of a wide variety. Most people required treatment and have persistent thyroid dysfunction many years after treatment. The minority were severe. Careful pro-active surveillance is required to prevent and treat these complications promptly.

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Introduction Alemtuzumab (Campath-1H), the first humanised monoclonal antibody, is emerging as the most effective disease modifying treatment for multiple sclerosis (MS). One common side effect is thyroid gland disturbance. However, despite use in clinical trials and off-licence as a compassionate treatment, little is known about the spectrum, clinical aspects, and treatment requirements of Campath induced thyroid dysfunction.

Aim To characterise the thyroid complications of the Plymouth Hospitals Campath cohort.

Method Hospital notes from all people with MS treated with Campath, were examined in chronological order (since 2002). Thyroid complications were characterised clinically, biochemically and immunologically.

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There is increasing evidence for genetic contribution to aetiology of multiple sclerosis (MS) and disease phenotype. The prolonged clinical course in MS limits collection of longitudinal phenotypic data. Alternative approaches include MS Severity Scale (MSSS), or extremes of outcome (EOO) comparisons. We have studied phenotypic impact of 14 non-HLA disease associated single nucleotide polymorphisms (SNPs) in a population with detailed longitudinal clinical data. Genotypes were analysed from 1007 MS patients followed for a mean of 10.4 years. Cox regression was used to test time to disability milestones (EDSS 4, 6, 8) and secondary progression (SP). Association with MSSS was tested using ANCOVA and EOO with χ². TYK2 (rs34536443) was associated with time to EDSS 4 (HR (95% CI) 1.3 (1.03,70), p=0.03) and EDSS 6 (HR 1.5 (1.10), p=0.01), and there was a trend towards association with MSSS (p=0.07) and EOO (p=0.05). KIF21B (rs12122721) was associated with time to EDSS 8 (HR 1.4 (1.02,9), p=0.03) and SP (HR 1.5 (1.15), p=0.02). CD88 (rs2500747) was associated with MSSS (p=0.03) and EOO (p=0.05), but was not associated with time to EDSS milestones. Non-HLA genotypes are unlikely to have a clinical impact on prediction of prognosis. In addition, use of different methodologies to analyse phenotype may produce conflicting results. There is a need for standard analytical methods to ensure that true phenotypic effects are detected.

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Communication and the doctor—patient relationship 5/76 (7%) PwMS and 52/74 (45%) PwMND had discussed such issues with a doctor or nurse. 16/77 (21%) PwMS and 38/72 (53%) PwMND wished to do so. 51% of both PwMS and PwMND considered it not a problem if their clinician was involved in assisted suicide. A further 25% PwMS and 21% PwMND felt it would not affect the treatment of their condition. The results highlight a need for better patient education and openness about end of life options, including advance decisions, and a greater exploration of these issues on a wider scale.

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129 SERUM IL-21 AS A BIOMARKER IN MULTIPLE SCLEROSIS
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30% of Alemtuzumab treated Multiple Sclerosis (MS) patients develop autoimmun disease (AID). Genetically determined pre-treatment serum IL-21 levels are a putative biomarker for this phenomenon and may be of clinical value, informing treatment choice and providing insights into patterns of disease expression and co-morbidity in MS. We evaluated IL-21 levels in sera of 42 normal controls and 248 MS patients; including 63 patients with highly active MS (HAMS), 43 of whom had been treated with Alemtuzumab, 36 age/sex matched disease controls, 36 patients seen serially during and after relapse and 59 with progressive disease. IL-21 concentrations were correlated with disease type, pre-treatment and in longitudinal samples were stable, varying by >10% in both relapsing and non-relapsing patient groups. There was an exponential association between IL-21 and MARR (r²=0.56, p=0.05). Levels were higher in patients with HAMS than other patient groups or controls (686 pg/ml vs 286 pg/ml and 241 pg/ml, p<0.001). High IL-21 levels (>550 pg/ml) were specific (95%) but non-sensitive (24%) for HAMS. 14/62 Alemtuzumab treated patients developed AID and high pre-treatment serum levels predicted this with high sensitivity (86%) and specificity (90%). This study confirms a role for serum IL21 levels as a pre-treatment biomarker for post-Alemtuzumab AID and suggests an association between IL-21 expression and MS relapse activity.

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128 QUANTIFICATION OF GLUTAMATE IN THE GREY MATTER AND ITS RELATIONSHIP WITH COGNITIVE PERFORMANCE IN MULTIPLE SCLEROSIS
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We aim to assess whether the concentration of glutamate, an excitatory neurotransmitter, changes in the grey matter (GM) of patients with Multiple Sclerosis (MS), and whether it relates to cognitive dysfunction and disability. Single-voxel MRS was performed at 3T in 18 patients with relapsing-remitting MS [12 women, age 43.5 years, median EDSS 2.8] and 17 healthy subjects [11 women, age 39.7] in the right cingulate and parietal cortices, right hippocampus and thalamus. (Abstract 128 figure 1) Visual and verbal memory and speed of information processing were assessed. Patients showed significantly worse performance on the visual memory test, verbal learning, delayed verbal recall, and speed of information processing, compared to controls. Patients showed lower glutamate concentration in the cingulate and parietal cortices and in the hippocampus compared to controls. Patients showed significantly lower N-Acetyl-Aspartate levels in the thalamus and cortical GM, and reduced glutamate-glutamine, choline-containing compounds and creatine plus phosphocreatine levels in the cortical GM, compared to controls. Lower hippocampal glutamate levels correlated with worse visual memory. Reduced glutamate levels in the cingulate cortex and thalamus correlated with worse speed of processing and visual memory, respectively. We found reduced glutamate neurotransmission in the cortical and hippocampal regions, which was linked to cognitive impairment. Reduced levels of most of the metabolites in the cortical GM, together with normal Inositol, are in agreement with post-mortem findings of GM neuronal loss, modest glial proliferation, low degree of inflammation and energy metabolism.

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130 A PILOT STUDY OF A TIMED SHORT ADDITION TEST AS A TOOL FOR THE LONGITUDINAL STUDY OF COGNITIVE DYSFUNCTION IN MULTIPLE SCLEROSIS
doi:10.1136/jnnp-2011-301993.172

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Cognition is a routinely measured in Multiple Sclerosis (MS) clinical trials using the Paced Auditory Serial Addition Task (PASAT) which tests arithmetic processing via a 60 element, time-paced list of single digits for addition. PASAT provides validated, longitudinal data but is rarely used outside trials as it is time consuming and requires audio equipment not routinely available in clinics. A quick, simple alternative would offer the opportunity to collect data currently missing from most clinical and epidemiological studies. We have piloted a timed short addition test (TSAT) comprising 10 serial digit-pair additions of the integers 1–10, in a predetermined order with the number of correct answers and time taken to perform the test recorded; correlating its performance with PASAT as a longitudinal measure of cognition. A total of 219 observations were made in 42 patients with MS relapsing and non-relapsing patient groups. There was an exponential association between IL-21 and MARR (r²=0.56, p=0.05). Levels were higher in patients with HAMS than other patient groups or controls (686 pg/ml vs 286 pg/ml and 241 pg/ml, p<0.001). High IL-21 levels (>550 pg/ml) were specific (95%) but non-sensitive (24%) for HAMS. 14/62 Alemtuzumab treated patients developed AID and high pre-treatment serum levels predicted this with high sensitivity (86%) and specificity (90%). This study confirms a role for serum IL21 levels as a pre-treatment biomarker for post-Alemtuzumab AID and suggests an association between IL-21 expression and MS relapse activity.

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Cognition is a routinely measured in Multiple Sclerosis (MS) clinical trials using the Paced Auditory Serial Addition Task (PASAT) which tests arithmetic processing via a 60 element, time-paced list of single digits for addition. PASAT provides validated, longitudinal data but is rarely used outside trials as it is time consuming and requires audio equipment not routinely available in clinics. A quick, simple alternative would offer the opportunity to collect data currently missing from most clinical and epidemiological studies. We have piloted a timed short addition test (TSAT) comprising 10 serial digit-pair additions of the integers 1–10, in a predetermined order with the number of correct answers and time taken to perform the test recorded; correlating its performance with PASAT as a longitudinal measure of cognition. A total of 219 observations were made in 42 patients with MS relapsing and non-relapsing patient groups. There was an exponential association between IL-21 and MARR (r²=0.56, p=0.05). Levels were higher in patients with HAMS than other patient groups or controls (686 pg/ml vs 286 pg/ml and 241 pg/ml, p<0.001). High IL-21 levels (>550 pg/ml) were specific (95%) but non-sensitive (24%) for HAMS. 14/62 Alemtuzumab treated patients developed AID and high pre-treatment serum levels predicted this with high sensitivity (86%) and specificity (90%). This study confirms a role for serum IL21 levels as a pre-treatment biomarker for post-Alemtuzumab AID and suggests an association between IL-21 expression and MS relapse activity.

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127 Attitudes towards end of life issues among people with MS: a 360 survey

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