Longitudinal study of cerebral atrophy and inflammatory lesions in multiple sclerosis

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Objective: The purpose of this study is to determine whether there is a temporal relationship between contrast enhancing lesions and whole brain atrophy.
Background: The role of inflammatory lesions in the development of cerebral atrophy is unclear. Although several longitudinal studies have demonstrated a correlation between contrast enhancing lesions and *regional* atrophy measures (e.g. ventricular enlargement) numerous cross- sectional and longitudinal studies have failed to demonstrate a correlation between enhancing lesions and *whole brain atrophy*.
Methods: This retrospective, longitudinal study compared monthly contrast enhanced MRI activity and monthly measurements of brain fractional volume (BFV) over 5 (range 3-9) years in eleven clinically definite multiple sclerosis (CDMS) patients. All patients had active MRI scans at entry. A minimum of two new contrast enhancing lesions (CEL) on three sequential baseline MRI exams were required for inclusion. Patients were followed for a minimum of 6 months during a baseline (pretreatment) phase and subsequently followed during treatment with recombinant Interferonß (IFN) and various other immunomodulatory agents. Pre-and post contrast axial images were obtained using gadolinium (0.1mm/kg). Newly enhancing lesions were sequentially recorded on hardcopy films for each monthly examination. Lesions with persistent enhancement were recorded only once. The cumulative number of contrast enhancing lesions was determined by the equation: $\sum$ (new CEL $_{\text{month 0}}$ + new CEL $_{\text{month 1}}$ + new CEL $_{\text{month 2}}$….) where month 0 represented the first MRI exam at entry. Monthly BFV was determined on pre-contrast T1W images using a fully automated program. For BFV measurements, all T1Wscans were registered to the entry examination, which served as a mask image. Cumulative cerebral atrophy was measured as percent brain fractional volume change (PBVC) compared to the entry baseline scan. Statistical analysis used Spearman rank correlation coefficient (SRCC) and linear regression. $P < 0.05$ was considered statistically significant.
Results: The results demonstrate that the course of cerebral atrophy parallels that of contrast enhancing lesion accumulation and is not necessarily linear with time. The correlation between cumulative CEL and PBVC ranged from $R^2 = 0.587 - 0.725$ which suggests that a significant proportion of cerebral atrophy can be attributed to inflammatory lesion activity. Immunomodulatory agents that effectively reduce CEL accumulation also slowed the rate of atrophy.
Conclusions: Although this is a small study, the consistent findings in a heterogeneous group of patients treated with a variety of immunomodulatory agents, suggests that these
two outcome measures may prove clinically reliable in evaluating patient response to therapy.

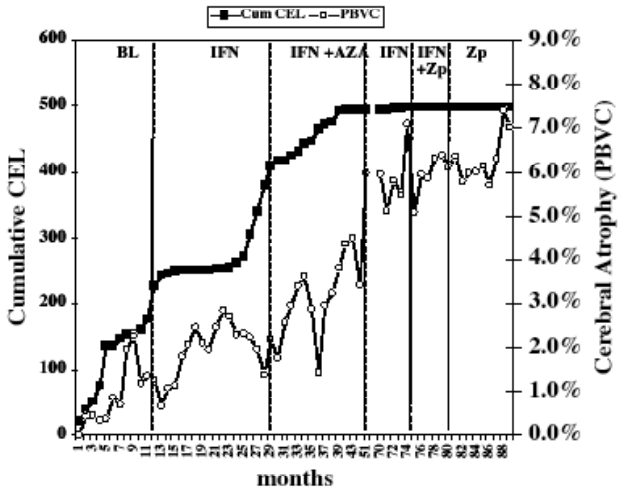

Fig.1.Parallel course of whole brain atrophy and cumulative contrast enhancing lesion number in a RRMS patient followed for 89 months with serial MRI examinations. Cumulative cerebral atrophy was measured monthly as percent brain volume change (PBVC) from entry MRI exam and the cumulative number of contrast enhancing lesions(CEL) were determined during a pretreatment, baseline (BL) period of 11 months, followed by treatment with InterferonB-1b (IFNB) alone or IFNB