

Brain-derived neurotrophic factor and Neurofilament light chain levels in multiple sclerosis patients treated with dimethylfumarate: a prospective observational study

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Aim: The study investigated the effect of Dimethyl fumarate (DMF) on Brain-derived neurotrophic factor (BDNF) and serum neurofilament light chain (sNfL) levels in RRMS patients.

Methods: Consecutive patients diagnosed with RRMS, referred to our MS center between March 2022 and November 2023, were enrolled if a first line therapy with DMF was started on the base of clinical and radiological features.

Demographic and clinical data included age at onset, sex, prior and current DMT, changes in annualized relapse rate, Expanded Disability Status Scale (EDSS) score, magnetic resonance imaging (MRI) data, collected at baseline clinical visits (T0) and after 12 months of DMF treatments (T1). Blood samples were drawn before starting therapy and 12 months later. Serum and supernatant from unstimulated peripheral blood mononuclear cells was collected and preserved at -80° until examination. sNfL levels and BDNF production was measured through ELLA System. Statistical significance was defined as $p < 0.05$.

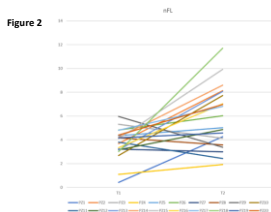
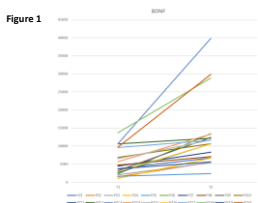
Results: We included 20 patients in the study (11 male), with a mean age of 37 ± 5 years, being all diagnosed with RRMS and with a median score of 1 ± 0.5 at the Expanded Disability Status Scale. 85% patients were newly diagnosed, 2 patients were shifted from copolymer to DMF after the appearance of a new brain T2-weighted lesions at MRI, one patient was shifted from fingolimod for side effects (table 1). 85% of Patients achieved the NEDA-3 status during the observational period.

Table 1. Patients demographic and clinical features at baseline.

	Overall population (n=20)
Demographics	
Age [years], mean \pm SD	37.0 \pm 5
Sex male, n (%)	11 (55)
Clinical Characteristics	
Age at onset, mean \pm SD	34.7 \pm 5.3
Naive Patients, n (%)	17 (85)
ARR, mean \pm SD	0.9 \pm 0.5
Contrast-enhancing lesions on the baseline MRI, n (%)	12 (60)
EDSS score, mean \pm SD	1 \pm 0.5

SD, standard deviation; ARR: annualized relapse rate; RI: Magnetic Resonance Imaging; NEDA-3: No Evidence of Disease Activity-3

In these patients we found a significant increase in BDNF production as from 12 months after starting therapy (3685 pg/ml vs 12631 pg/ml) ($p=0.001$) and a significant decrease of serum NfL (5,90 pg/ml vs 3,70 pg/ml) ($p=0.026$) (figure 1, 2).



Conclusion: Our study demonstrated that RRMS Patients who achieved NEDA-3 status after 12 months of DMF therapy showed higher levels of BDNF and lower levels of sNfL. Our data suggest that part of the neuroprotective and immunomodulatory effects of DMF in MS patients could be also mediated by the up-regulation of BDNF production.

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