

Neurofilament light chain and levels of fatigue are reduced by dimethyl fumarate – fatigue is not related to neuroaxonal damage

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Introduction:

No studies have prospectively investigated the relationship between levels of neurofilament light chain (NFL) and fatigue before and after treatment with dimethyl fumarate (DMF).

Objectives:

- (i) To analyze levels of NFL in blood and CSF from newly diagnosed untreated relapsing MS patients;
- (ii) to estimate fatigue and NFL, and their association, before and after DMF treatment.

Methods:

Patients were prospectively enrolled and treated with DMF for 12 months. CSF were collected at baseline (BL) (n=34), after 12 months (n=31), blood was collected at BL and 3, 6 and 12 months (n=185) and both blood and CSF from healthy controls (HC)(n=14). NFL concentrations were measured by Single Molecular Array (SiMoA). Fatigue was evaluated with Fatigue Scale of Motor and Cognitive Function (FSMC) and the Modified Fatigue Impact Scale (MFIS).

Results:

After 12 months of DMF treatment, NFL levels were on average reduced 72% (1340 pg/ml) in the CSF ($p < 0.0001$) and respectively 45% and 55% reduction in plasma levels after 6 months ($p < 0.01$) and 12 months ($p < 0.0001$) of DMF treatment compared to baseline and levels were similar to healthy controls. Patients were fatigued at baseline measured both by $MFIS_{BL}$ of $31.2 (\pm 20.4)$ and $FSMC_{BL}$ of $46.7 (\pm 20.8)$. MFIS scores demonstrated a significant reduction after treatment with DMF at $MFIS_3$: $7.85 (\pm 12.20; p = 0.003)$, $MFIS_6$: $7.75 (\pm 15.59; p = 0.0032)$ and $MFIS_{12}$: $8.40 (\pm 15.55; p = 0.0015)$. FSMC showed similar decrease at follow-up, however not significant. No correlation was found between NFL and levels of FSMC and MFIS and their respective subscales.

Conclusions:

DMF reduces levels of NFL both in blood and CSF suggesting that DMF reduces neuroaxonal damage in patients with multiple sclerosis. Fatigue levels were also decreased significantly after DMF treatment. No correlation between NFL and fatigue could be demonstrated suggesting that levels of fatigue in MS are not related to neuroaxonal damage.

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