

NEUROFILAMENT LIGHT CHAIN AND LEVELS OF FATIGUE ARE REDUCED BY DIMETHYL FUMARATE – FATIGUE IS NOT RELATED TO NEUROAXONAL DAMAGE



INTRODUCTION & OBJECTIVES

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

(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).

Patients RRMS	Female	Age (± SD)	EDSS (± SD)
N = 52	42 (80.8%)	33 ± 8.04	1.73 ± 0.91

Table 1. Baseline Demographics. Gender, Age and Expanded Disability Status Scale (EDSS) ± Standard Deviation (SD) at the time of inclusion.

RESULTS

- After 12 months of DMF treatment
 - CSF: NFL levels were on average reduced 72% (1340 pg/ml) in the CSF (p<0.0001)
 - Blood: 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(±20.4) and FSMC_{BL} of 46.7 (±20.8). MFIS scores demonstrated a significant reduction after treatment with DMF at MFIS₃: 7.85 (±12.20; p=0.003), MFIS₆: 7.75 (±15.59; p=0.0032) and MFIS₁₂: 8.40 (±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.
- No difference could be found in levels of NFL when stratified in subgroups based on level of fatigue that improved, worsened or stabilized.

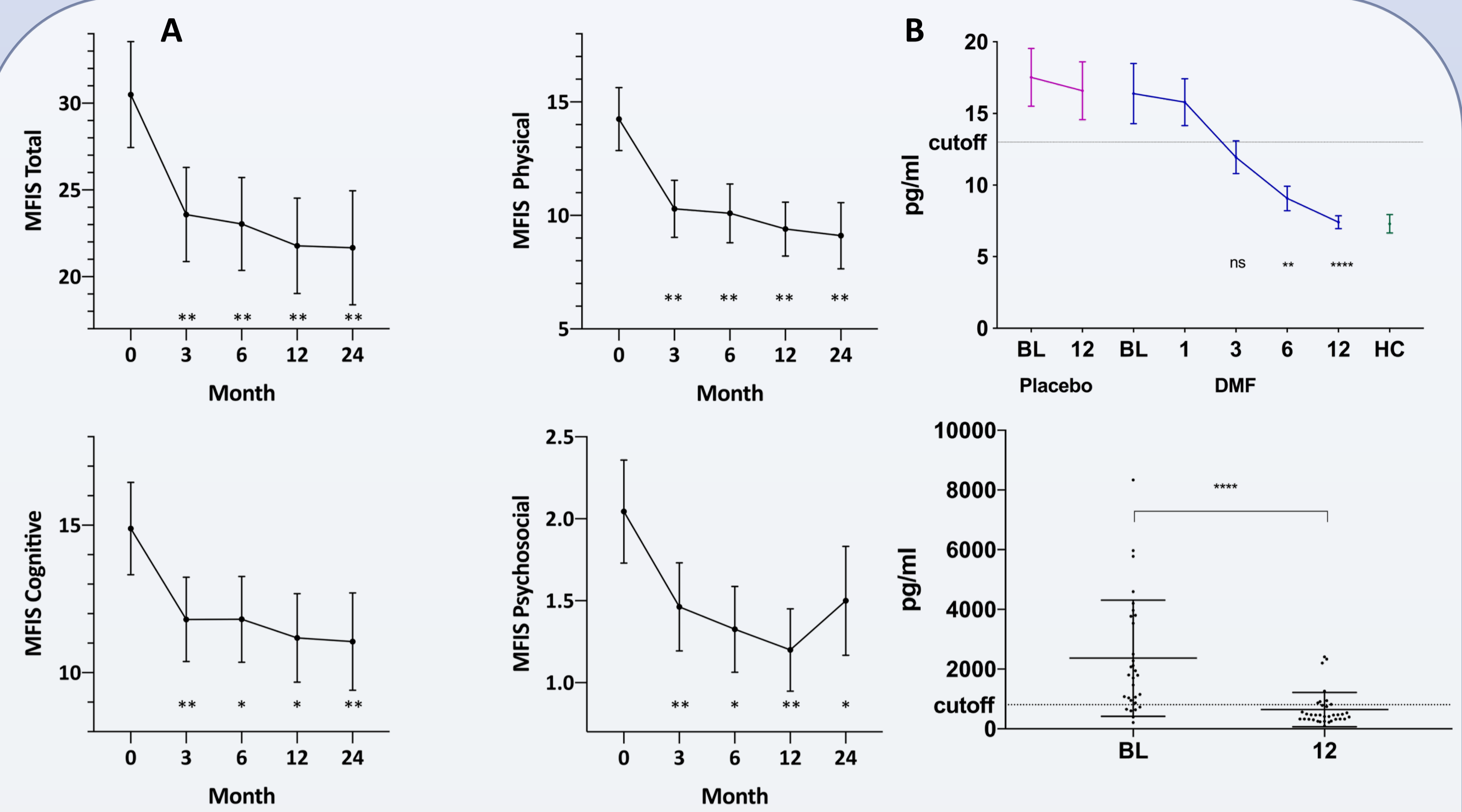


Figure 1.

A The Modified Fatigue Impact Scale (MFIS) mean score in total and in physical, cognitive and psychosocial subscores at baseline, 3, 6, 12 and 24 months illustrated with error bars (Standard Error of the Mean).

B Upper figure: Neurofilament light chain (NFL) in plasma compared to placebo and healthy controls (HC) at baseline (BL) and after treatment with dimethyl fumarate (DMF). Number indicate months after initiation of treatment. Lower figure: NFL in CSF at BL and after 12 months of treatment with DMF.

Significant mean decrease marked with * (p<0.05), ** (p<0.01) and **** (p<0.0001).

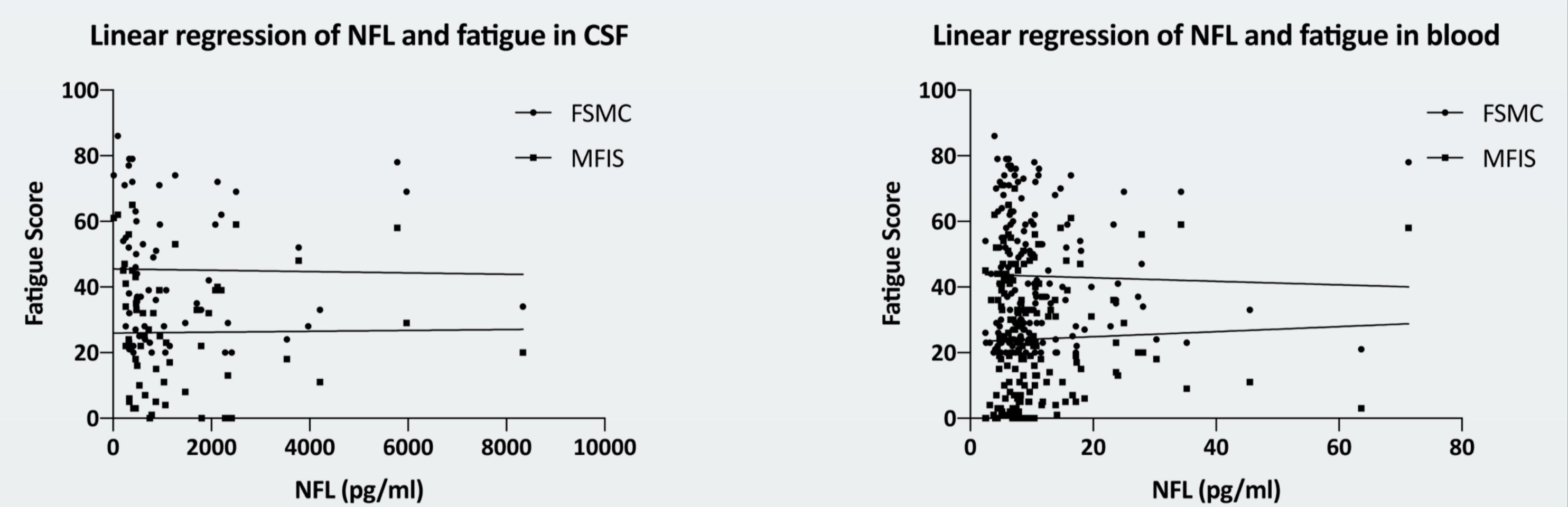


Figure 2. Linear Regression of fatigue levels and Neurofilament light chain (NFL) levels in CSF and blood

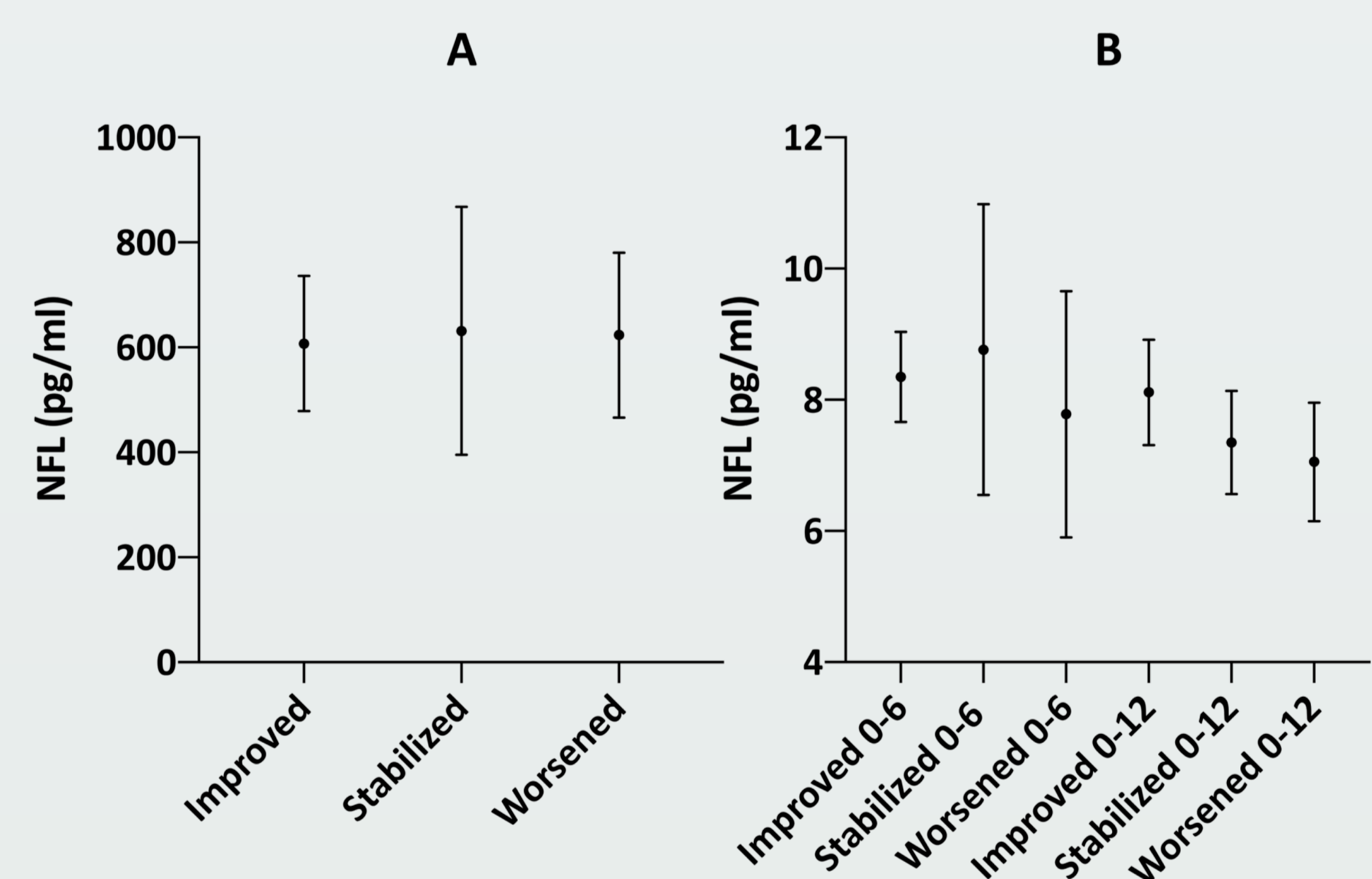


Figure 3.

Neurofilament light chain (NFL) levels in CSF (A) and blood (B) stratified into subgroups; if fatigue improved, stabilized or worsened compared to baseline and after treatment with dimethyl fumarate. NFL levels in CSF levels at 12 months and blood levels at 6 and 12 months after treatment with dimethyl fumarate.

CONCLUSION

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.

ACKNOWLEDGEMENTS

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