Immunophenotyping of Depression and Fatigue in Relapsing-Remitting Multiple Sclerosis (RRMS) Patients Treated with Dimethyl Fumarate
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**Objective:**
This study aims to characterize the immune-phenotype of peripheral blood mononuclear cell (PBMC) subsets in MS patients who do or do not have depression and fatigue and identify cellular biomarkers that can be used to screen for patients who suffer from them.

**Background:**
Depression and fatigue are common and severe symptoms in patients with multiple sclerosis (MS). While many factors play a role in the development of depression and fatigue, both have been associated with increased inflammatory activation in the immune system.

**Design/Methods:**
Multi-colour flow cytometry panels were designed to identify up to 50 peripheral blood lymphocyte subpopulations. The severity of fatigue and depression were measured with the Fatigue Severity Scale (FSS) and the Hospital Anxiety and Depression Scale (HADS). Comparisons were done between patients treated with dimethyl fumarate (DMF) who did and didn’t had depression and fatigue. Correlations of the PBMC subpopulations were also done with both FSS and HADS-D score.

**Results:**
There is a significant positive correlation between the depression and fatigue scores. Depressed patients had significantly lower number of T cells than those without depression. CD8\textsuperscript{+} Treg were shown to be significantly higher in depressed patients. HADS-D score also strongly correlated with both CD4\textsuperscript{+} and CD8\textsuperscript{+} Treg counts. Fatigue scores (FSS) had a significant positive correlation with the number of classical monocytes. Both CD4\textsuperscript{+} and CD8\textsuperscript{+} Tregs also positively correlated with FSS scores as well as the CD4\textsuperscript{+}CD45RA\textsuperscript{-}CD62L\textsuperscript{+} subpopulation.

**Conclusions:**
Our results show that depression and fatigue in MS patients treated with DMF are associated with an increased level of regulatory T cells, as previously shown in studies involving depressed patients without MS. This may be a result of the immune system compensating for the proinflammatory environment, which suggests that even in MS depressed and fatigued patients have a more inflammatory immune environment than those without the two symptoms.