Coagulation/complement activation and cerebral hypoperfusion in relapsing-remitting multiple sclerosis

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Background Multiple sclerosis (MS) is an inflammatory disease of the central nervous system. It has been demonstrated that not only adaptive immunity but also innate immune system plays a relevant role in MS pathogenesis (Gandhi 2010; Mayo 2012).
There are several studies confirming platelet (Horstman 2010; Nurden 2011; Behari 2013) and complement (Horstman 2011; Veerhuis 2011; Ingram 2012) involvement in MS, having an important role in the innate immune response by linking inflammation and coagulation.
Moreover, decreased cerebral blood volume and flow, as well as its prolonged mean transit time, have been demonstrated in all forms of MS, both in white and grey matter, by dynamic susceptibility contrast-enhanced MRI (Adhya 2006, Inglese 2007, Varga 2009).
The aim of our study is to evaluate the serum/plasma levels of coagulation/complement factors in relapsing MS patients compared to remitting ones and to healthy controls, and to assess the presence of brain hemodynamic changes of patients in order to correlate their coagulation status with MRI perfusion data.

Materials and Methods
Informed and consenting MS pts (1° group: REL; 2° group: REM) and age- and sex-matched CTR (3° group) will be enrolled in the study. Patients' level of disability will be evaluated using the EDSS score and MSFC score.
All pts and CTR will be tested for complement/coagulation and soluble markers of endothelial damage assays, all pts will undergo dynamic susceptibility contrast-enhanced MRI using a 3.0-T scanner to evaluate CBF, CBV and MTT, lesion number and volume.

Sample size calculation
Overall 90 subjects (30 for each group) will be enrolled in order to compare the level of complement C4a (Ingram 2012). By using the ANOVA test, this sample size will allow to detect effect size values [delta=(miA–miB)/sigma] equal to at least 0.71, with a statistical power of 80%, to a level of significance of 5%.

Statistical Analysis
To measure differences between MS pts and CTR unpaired t-tests will be used; univariate correlations will be calculated using Spearman rank correlation coefficient.

Impact and Translational Implications Identifying a link between activation of coagulation/complement system and cerebral hypoperfusion in MS pts could lead to the development of new effective therapeutic strategies for MS pts. Even if the activation of coagulation system, linked to innate immunity, is a mandatory process following different types of tissue damage and it is not the primary cause of the formation of demyelinating plaque, interfering with coagulation system could represent a new therapeutic target in MS.