Multiple sclerosis and depression comorbidity: deciphering the role of early-life adversities

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Multiple sclerosis (MS) is an inflammatory, demyelinating disease of the central nervous system, often accompanied by psychological changes that lessen patient quality of life. Indeed, in addition to the difficulties associated with the disease itself, approximately one-quarter of MS patients often show a marked mood reduction that leads to the development of depression. Despite several epidemiological studies indicating high comorbidity between MS and depression, the knowledge of the biology of these two disease has not led to an improvement in the overall impact of pharmacotherapy for MS-associated depression and many MS patients report that their psychosocial needs are not adequately addressed, thus generating a critical unmet need. Based on these considerations, the overall aim of our study was to investigate the association between MS and depression evaluating the influence of early life stress events –well-established risk factors for depression- on the development of MS. Specifically, we used a well-characterized animal model of MS, the EAE-induced mice, which was generated in control mice as well as in mice prenatally exposed to stress. Given that both depression and MS affect women twice as often as men, EAE was induced by immunization with MOG35-55/CFA and treatment with pertussin toxin (PTX) at 0 and 2 days post-immunization (DPI) in eight-week-old female C57B/L6 mice born from control or stressed dams exposed during last days of gestation (from gestational day 14 until delivery) to restraint stress. Next, starting from DPI 8, we performed several behavioral tests to evaluate the mutual impact of stress and MS.

By using the sucrose intake test, we found that prenatal stress induced an anhedonic-like phenotype only in the EAE-mice, an effect that -although not statistical significant- is suggestive of an interaction between the two condition. This hypothesis was also supported by the analysis of the EAE clinical score that was daily monitored. Indeed we found that prenatal stress was able to increase the severity of the clinical scores, particularly in the last part of the acute phase and during the chronic phase, without any impact on the temporal insurgence of the EAE-phenotype.

These results clearly indicate an interplay between EAE-induction and prenatal stress exposure, suggesting this combined model as a great promising candidate in the study of depression-associated MS. Further analyses are demanded to better characterize the feature of EAE and PNS combination, particularly at molecular level.

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