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Multiple sclerosis: Protection by the male hormones

Richard Béliveau

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A recent study reports that androgens are needed to regenerate the myelin sheath that is destroyed in multiple sclerosis, which could pave the way for better treatment of this disease.

Multiple sclerosis (MS) is an autoimmune disease, characterized by inflammatory attacks leading to the destruction of the myelin which coats the neurons of the central nervous system.

The ensuing nerve damage causes several motor, sensory or visual disorders that considerably reduce the quality of life of those affected.

In 85% of cases, MS presents in a relapsing-remitting form, i.e. the symptoms appear suddenly, then totally or partially disappear in the following weeks. This recovery is made possible by the spontaneous regeneration of myelin that has been destroyed.

However, in a proportion of patients (15%), this myelin repair process becomes ineffective and the neurological symptoms of the disease then gradually worsen over the years, without the possibility of remission.

Although current treatments can reduce the frequency and the severity of inflammatory flare-ups for relapsing forms of MS, they nevertheless remain ineffective against progressive forms of the disease.

HORMONE CONTROL

At least three features of MS suggest that hormones could play an important role in the development of this disease (1):

1) the incidence of MS is much more frequent in women, with a ratio of three women to one man who are affected by the disease;

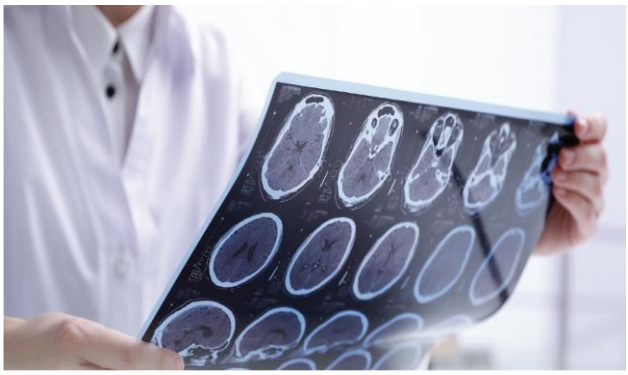
2) hormonal variations associated with certain conditions (the pregnancy, in particular) have an influence on disease recurrence rates;

3) older men, who have lower androgen levels, develop more severe forms of MS. This therefore suggests that circulating levels of estrogens or androgens participate in the myelin repair process.

ANTI-INFLAMMATORY AND REPAIRING ANDROGENS

The role of androgens seems particularly important: it has indeed been observed that androgens protect the neurons of the central nervous system of men with relapsing-remitting forms of MS and induce the regeneration of the sheaths of myelin destroyed.

Even if androgens are present in much lower quantities (10-20 times less) in women, a recent study suggests that they still play a crucial role in the repair of the myelin destroyed by the immune disorders responsible for the SP (2).



By examining biopsies from patients with MS,researchers first observed that the nervous tissue of women expresses high amounts of the specific androgen receptor, suggesting an important role of these hormones in neuronal functioning.

This was confirmed by a biochemical analysis showing that androgens increase the activity of genes involved in maintaining the integrity of neurons and the production of myelin, while reducing that of genes responsible for the overactivation of immunity.

In women, the researchers also observed that androgens caused a drastic decrease in the level of local inflammation, in areas where myelin is destroyed, which could create an anti-inflammatory climate that slows down the progression of the disease.

The use of appropriate doses of androgens in women with MS could therefore represent a new approach to reduce the frequency of inflammatory flare-ups responsible for relapsing forms of MS.

(1) Voskuhl RR and Gold SM. Sex-related factors in multiple sclerosis susceptibility and progression. Nat. Rev. Neurol. 2012; 8: 255-263.

(2) Zahaf A et al. Androgens show sex-dependent differences in myelination in immune and non-immune murine models of CNS demyelination. Nat. Commun. 2023 ; 14 : 1592.

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