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Elisabeth Traiffort

Inserm-Paris Saclay University, Kremlin-Bicêtre, France

Androgens: Their unexpected role in females with multiple sclerosis

Abstract:

Multiple sclerosis (MS), an inflammatory and neurodegenerative disease, is known to be the most common demyelinating disease of the central nervous system (CNS) and the main cause of non-traumatic disability in young adults. This pathology is sexually dimorphic with a three-fold higher prevalence in women. The female sex hormones (estrogens, progestagens) have previously been characterized as neuroprotective and remyelinating in the brain or spinal cord derived from various models of this disease. However, females also synthesize small amounts of male sex hormones or androgens. Well-characterized in males, the role of androgens still remained widely unexplored in females. Recently, we addressed the question to determine if androgens could be involved in the spontaneous regeneration of myelin that eventually fails in MS patients, mostly in the late stages of the disease, which results in worsening and irreversibility of the neurological symptoms. Using pharmacological and genetic approaches as well as demyelinated tissues from various models of the disease or patients with MS, we detected unexpectedly and exclusively in females, a high level of the main receptor of androgens (AR) in the CNS areas that display myelin loss. AR expression predominates in microglia, the resident immune cells of the CNS. We provide evidence for a synergism between the effects induced by male and female sex hormones and show that only androgens drive microglia response towards tissue regeneration. In the demyelinated mouse spinal cords, transcriptomic analyses showed that, regardless of the sex, androgens up-regulate genes related to neuronal function integrity and myelin production. However, only in females, androgens are able to down-regulate genes related to the immune system and thus to decrease neuroinflammation. Globally, our data indicate that normalizing androgen levels in females is required for proper regeneration of myelin and reduction of neuroinflammation. Moreover, therapeutic approaches of demyelinating diseases need to consider male-female differences.

Biography: Elisabeth Traiffort has completed her PhD from Paris University (France) after several years spent as a pharmacist in Assistance Publique-Hôpitaux de Paris (AP-HP Hospitals), the largest hospital system in Europe and one of the largest in the world. She is responsible for the Research Team 'Myelinopathies' in the Inserm-Paris Saclay University Laboratory 'NeuroBicêtre' and has contributed to around a hundred publications in recognized journals.