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Effects of progesterone and nestorone on myelin

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Multiple Sclerosis (MS) is a complex neurodegenerative disorder of brain and spinal cord involving a dysfunctional immune-mediated process that effects white and grey matter lesions in the central nervous system.

The natural history of MS suggests that female sex hormones have a beneficial influence on slowing the progression of the disease. Progesterone (P) and some selective progestins such as Nestorone® (NES) have shown myelin regeneration in preclinical studies and may be promising candidates for use in the treatment of MS.

NES, a synthetic, non-androgenic derivative of 19 norprogesterone, is 100 times more potent than P in terms of progestational bioactivity, and has been extensively studied for its use in contraception. NES has a high selectivity for progesterone receptors (PR) and does not bind to androgen or estrogen receptors.

Experiments both in vitro and in vivo showed that NES stimulate oligodendrocytes and myelin repair and decrease the severity of the Experimental Autoimmune Encephalitis (EAE) in mice, an animal model for MS. The remyelinating effect of P and NES were mediated via progesterone receptors (PR) and NES showed consistent positive responses in the same dose range. In contrast to P, NES and its reduced metabolites do not activate the GABAA Receptors (R), suggesting that the myelin regenerative effects of NES are mediated via PR binding and not via the GABAAR.

Our data suggest that NES by protecting axonal networks and stimulating myelin repair, may prove useful as a possible adjuvant therapy for men and women with MS.

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