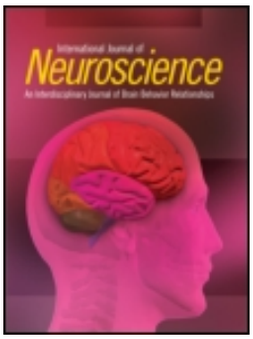

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Letter to the Editor

PROLACTIN SECRETION IN MULTIPLE SCLEROSIS

(Received March 1, 1991)

To The Editor:

Multiple sclerosis (MS), a chronic demyelinating disease of young adults, is characterized clinically by episodes of focal disorder involving the optic nerves, brainstem, cerebellum, and spinal cord, which remit to a varying extent and recur over a period of many years (Adams and Victor, 1985; Weinshenker and Ebers, 1987). The clinical manifestations are protean, being determined by the varied locations and extent of the foci of demyelination. Pathologically, there is an inflammatory response observed in the central nervous system consisting predominantly of activated T-cell lymphocytes and macrophages (Prineas et al,, 1978) accompanied by a local immune reaction resulting in the secretion of interleukins and in the synthesis of oligoclonal immunoglobulin (IgG) by plasma cells (Frick and Scheid-Seydel, 1958). Foci of demyelination affect primarily the white matter of the brain and spinal cord. It has been hypothesized that the loss of suppression of or imbalance in the immune system may play a crucial role in the pathophysiology of this disease (Waksman and Reynolds, 1984).

The etiology and pathogenesis of MS are unknown. Epidemiological data suggest that MS is related to some as yet unidentified environmental factor that is encountered in childhood and which, after years of latency, either produces the disease or contributes to its presentation (Adams and Victor, 1985). Research in the past decade suggests that this environmental factor may be of viral origin (McFarlin and McFarland, 1982), triggering an autoimmune process directed against myelin (Weiner and Hauser, 1982; Waksman and Reynolds, 1984). Furthermore, the parallel in histopathological findings and in clinical symptoms of MS to chronic relapsing experimental allergic encephalomyelitis (EAE) (Wisniewski and Keith, 1977), a T cell-mediated autoimmune disease, has led to the concept of MS as an autoimmune disease (Wisniewski and Keith, 1977).

There is increasing support for the view that a bidirectional communication exists between endocrine systems and the immune system (Sapolsky et al., 1987; Bernton et al., 1987; Rey et al., 1987) and that hypothalamic-pituitary neuroendocrine systems are involved in the regulation of immune responses (Hadden, 1987; Sapolsky et al., 1987; Berkenbosch et al., 1987). For instance, glucocorticoid-associated immunoregulatory mechanisms are implicated in a constant surveillance of the activity of immune cells (Rey et al., 1987). In addition, opioid peptides, sex steroids, prolactin, and catecholamines, and serotonin (5-HT) affect immune competence (McCann et al., 1987; Devoino et al., 1988). Conversely, immune cell-derived products such as lymphokines and monokines have been proposed to influence brain function in part via the hypothalamic-pituitary endocrine systems (Berkenbosch et al., 1987).

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In experimental animals, ablation of the anterior hypothalamus inhibits antibody response to antigens, delayed-type hypersensitivity to tuberculin, and anaphylaxis (Macris et al., 1976). Furthermore, electrolytic destruction of the anterior hypothalamus in rats has been reported to prevent the development of EAE (Abramsky et al., 1987). These findings indicate hypothalamic-pituitary modulatory effects on the immune system and on autoimmune responses of the central nervous system (CNS).

Among the pituitary hormones, growth hormone (GH) and prolactin have been particularly implicated in immunoregulation (Kelley et al., 1987). Lymphoid cells have been shown to possess receptors for both GH and prolactin (cf. Kelley et al., 1987). Moreover, prolactin has been demonstrated to augment a variety of immune events including antibody synthesis (Nagy et al., 1983; Nagy et al., 1985; Hiestand et al., 1986) and prolactin secreting pituitary epithelial cells augment thymic functions in aged rats (Kelley et al., 1987).

Although the demyelinating lesions of MS occur in multiple areas of the CNS, a periventricular localization is characteristic (Adams and Victor, 1985). Periventricular lesions may disrupt the inhibitory hypothalamic dopaminergic control of prolactin secretion leading to increased plasma prolactin levels in MS patients. Since prolactin augments a variety of immune responses (cf. Kelley et al., 1987), increased prolactin secretion might exacerbate symptoms of the disease and possibly hasten its rate of progression.

To investigate whether acute exacerbation of MS symptoms is associated with increased prolactin secretion, we evaluated serum prolactin levels in a cohort of 14 MS patients who were admitted consecutively for acute exacerbation of symptoms to a neurological service in Bay City, Michigan. The sample included 5 men and 9 women (mean age = 40.0 years, SD = 6.4; mean age of onset 28.0 years, SD = 10.6; mean duration of illness 12.0 years, SD = 11.8). None of the patients was taking neuroleptic drugs, bromocriptine, or oral contraceptives during the time of evaluation.

The diagnosis of definite MS was established on the basis of clinical criteria and supporting laboratory documentation including CSF analysis (oligoclonal bands), visual, auditory, and somatosensory evoked potential studies, CT scan, and magnetic resonance imaging (MRI) (Poser et al., 1983). Venipuncture for prolactin levels was performed at approximately 10.00 a.m. with the nursing staff and laboratory technicians blind to clinical information and hypotheses of the study.

In the sample only 3 (21.4%) patients had serum prolactin level above the normal range (mean = 59.0 ng/ml, SD = 19.0) (normal level = 0–23 ng/ml). These findings are in accordance with a previous report demonstrating normal serum prolactin levels in 37 out of 40 chronic progressive MS patients (Reder and Lowy, 1989). In our sample, serum prolactin status was unrelated to patient's age, sex ($\chi^2 = 2.12$), age of onset of illness, duration of illness, predominant neurological involvement (i.e., ocular, cerebellar, spinal, or generalized forms), or clinical course of the disease (i.e., chronic progressive versus relapsing-remitting).

We conclude, therefore, that although periventricular lesions are characteristic of MS and were demonstrated on MRI in 11 (78.5%) of our patients, the disease is not associated with major disruption of prolactin secretion and that elevations of serum prolactin levels do not contribute significantly to the augmentation of immune responses seen in active MS. Furthermore, it is unlikely that the dramatic rise of prolactin secretion during pregnancy (Martin and Reichlin, 1987) underlies the reported decline in the rate of exacerbation of MS during this period (cf. Reder and Lowy, 1989). Likewise, it seems unlikely that elevation of serum prolactin levels could be

related to the reported increased rate of exacerbation of MS during the post partum period (Schapira et al., 1966; Goldstein, 1966; Birk et al., 1988).

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