INTRODUCTION TO

NEUROSTEROIDS IN PAIN CARE

NEW TERM, NEW CONCEPT, NEW HOPE

CHAPTER 3
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BRINGING A NEW DIMENSION TO PAIN CARE

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Hormones & Pain Care Information Network

Some interesting hormones have picked up the new title, neurosteroids.[1,2] For us it's a new frontier and an exciting one, as the neurosteroids give us a great hope as adjuncts to our current pain treatment methods. The term neurosteroid designates bioactive steroids that are endogenously synthesized in neurons and/or glial cells in the central nervous system (CNS) and peripheral nervous system (PNS). The chemical structure of neurosteroids is identical to those produced in the adrenals and gonads, but the main criteria to be called a neurosteroid is that its production in the CNS or PNS is independent from the production in these glands and of the stimulatory activity of the hypothalamic releasing hormones and the stimulatory hormones of the pituitary, adrenocorticotropin (ACTH), follicle stimulating hormone (FSH), and luteinizing hormone (LH). There are three neurosteroids which are of critical importance to the control and even the cure of pain: pregnenolone, progesterone, and dehydroepiandrosterone (DHEA). (Table Two) A close relative of progesterone, allopregnanolone, is synthesized in the CNS but apparently not in adrenal or gonadal tissue.[3] Estrogen may be synthesized in the spinal cord and may be included as a neurosteroid in the future.[1]

Multiple animal studies are quite clear.[4-9] All three neurosteroids provide neuroprotection and neurogenesis when there is experimental, intentional injury to laboratory animals.[8-10] (Table Two) Neurosteroids modulate nervous system activity and pain control by acting through various membrane receptors including $GABA_a$, NMDA, and sigma.[11-14] In addition, the neurosteroids have anti-fatigue and memory enhancement properties[1-4]. To date, a limited number of clinical studies show that neurosteroids may reduce pain and some troubling symptoms such as allodynia.[6] This author has begun routine serum testing for these three neurosteroids and administering them in patients who have low serum levels. In my open-label trials, patients generally report clinical improvement in some symptoms such as less baseline pain, fewer flares, less allodynia, less fatigue, and better mental functions.[15] Opioid use is reduced in most patients. DHEA has been particularly useful in females who take opioids and have low testosterone levels. It is known to raise testosterone levels.

The proportional contribution of CNS, PNS, and adrenal-gonadal production to serum levels of pregnenolone, progesterone, and DHEA is unknown, but testing in my patients suggests that CNS and PNS production contributes to the overall serum pool. This author has observed severe

pain patients who have low serum levels of adrenocorticotropin (ACTH) and cortisol but have normal levels of pregnenolone and DHEA which shouldn't occur unless there is a serum contribution from other than the adrenals. I have observed the reverse which suggests there may be CNS and PNS suppression of neurosteroids in the face of normal adrenal production. Given the critical pain control functions of these three neurosteroids, it appears only common sense and logical to maintain serum homeostasis of them by simple, systemic administration.

To me the basic science studies and my clinical experience, to date, are very encouraging and provide new hope in pain therapeutics. The purpose of this note is to encourage interest in the neurosteroids. Keep in mind the profoundness of the discovery that the brain itself is an endocrine gland that produces its own pregnenolone, progesterone, and DHEA for neuroprotection, neurogenesis, and other pain-related functions.[1,2] We have to pursue the testing and administration of neurosteroids.

TABLE ONE

NEW VOCABULARY

NEUROSTEROIDS

A common producer in the CNS that has a steroid ring structure and is not under control of the pituitary-adrenal-gonadal axis.

NEUROGENESIS

Growth of nerve tissue.

NEUROPROTECTION

Keeps nerve tissue from degenerating when there is injury.

NEUROHORMONE

A hormone that acts on nerve tissue.

ANABOLIC NEUROGENIC

A compound that causes nerve growth.

TABLE TWO

NEUROSTEROIDS	PAIN-RELATED FUNCTIONS
PREGNENOLONE	NEUROPROTECTION
PROGESTERONE	NEUROGENESIS
DEHYDROEPIANDROSTERONE (DHEA)	RECEPTOR REGULATION
	NERVE CONDUCTION

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