Can Hormones Subtype Depression?

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In 1974, fortified with a residency in psychiatry and a fellowship in neuroendocrinology, I took a job at Brown University's new medical school, set up shop at the Providence Veterans Administration (VA) Medical Center, and was ready to take on the mind-brain problem. For two years I scrutinized the relationship between hormones and psychological state in healthy young men—in retrospect a maneuver designed to stave off the booby traps of clinical research. But my innocence was short-lived. In 1976 Bernard I. Carroll and his associates reported that among depressed patients, resistance to dexamethasone suppression appeared to be associated with primary—opposed to secondary—depression, older age, frequent depressive episodes, cognitive impairment, good improvement with hospitalization, and response to specific antidepressants. Thus, heightened pituitary-adrenocortical activity may characterize a depressive subtype with a distinct pathophysiology, clinical course, and treatment response. [The SCF and SSCF indicate that this paper has been cited in over 80 publications.]

The possibility that measures of pituitary-adrenocortical function identify meaningful subtypes of depressive illness continues to be explored. In 1984, in the context of an antidepressant study, Michael Arato, a visiting professor from Hungary; Ram K. Shrivastava, a collaborator from New York; and I began to look for features of depression—symptoms, illness course, cognitive function, age, treatment response—associated with normal and abnormal pituitary-adrenocortical activity. When three separate studies had been completed, Brandon and I decided to summarize our observations in light of the possibility that pituitary-adrenocortical abnormality characterizes a pathophysiologically discrete depressive subtype. So we wrote this paper.

I was surprised to hear that, by whatever circuitous route, our paper has achieved Citation Classic status. Surprised and gratified. I was pleased with this paper when we wrote it and I still am. It provided an opportunity to present evidence in support of a fundamental proposition. I fear, however, that our paper is cited not because of its weighty implications, but because it appeared before the outpour of DST reports and offered data on a number of DST matters—age, treatment response, severity—that we thought we had discovered.

The informal collaborations that brought off the studies reported in this paper have evolved into an affective disorders research group. Now a greater range of projects—ECT, psychosocial treatment, “biology” of suicide, family dynamics—are on the table, we’re a bit larger, and meet regularly. But there’s no written agenda and in most other ways we are as untidy as ever. The VA Medical Center’s psychiatric ward has become a center for clinical psychiatric research.

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