CC/NUMBER 32
AUGUST 7, 1989

This Week's Citation Classic®

Matussek N, Ackenheil M, Hippius H, Müller F, Schröder H-Th, Schultes H & Wasilewski B. Effect of clonidine on growth hormone release in psychiatric patients and controls. *Psychiat. Res.* 2:25-36, 1980.
[Department of Neurochemistry, Psychiatric Hospital, University of Munich, and Alexander-von-Humboldt-Stiftung, Munich, Federal Republic of Germany]

Endogenous depressive patients, in comparison to normal controls, nonendogenous, and schizophrenic patients, show a blunted growth hormone response to clonidine. We interpreted our findings as being due to a subsensitivity of postsynaptic α_2-adrenoceptors in endogenous depression. [The *SCI*® and *SSCI*® indicate that this paper has been cited in over 150 publications.]

α_2-Adrenoceptor Subsensitivity in Depression

Norbert Matussek
Department of Neurochemistry
Psychiatric Hospital
University of Munich
D-8000 Munich 2
Federal Republic of Germany

May 8, 1989

During the 1960s I had the opportunity to work for one year with B.B. Brodie, a most stimulating scientist at the National Institutes of Health. During that time I started to study the mechanism of action of antidepressant drugs. Initiated by these first studies, some other biological psychiatrists and I were increasingly convinced that a norepinephrine deficit in nerve endings was the main reason for the manifestation of a depressive syndrome in humans—a hypothesis that could however not be confirmed.

The introduction of neuroendocrine studies offered possibilities for studying brain functions in living human beings. About that time I moved from the Max-Planck-Institute of Psychiatry to work with Professor H. Hippius, chief of the Psychiatric Clinic of the University of Munich, where I had excellent circumstances for clinical investigations.

Starting with the amphetamine growth hormone (GH) stimulation test, in collaboration with G. Langer, a research fellow from Vienna, we found a blunted GH response to amphetamine in endogenous depressive patients in comparison to controls.[1] However, the question whether pre- or postsynaptic disturbances were the main pathophysiological correlate could not be answered. In order to prove a postsynaptic α_2-adrenoceptor subsensitivity, we used the recently developed antihypertensive drug, the α-adrenoceptor agonist clonidine (CLO), to stimulate GH secretion. Obviously, the CLO-GH stimulation test had to be first investigated in untreated, depressed patients. These are however admitted very seldom to our clinic and thus are rare like jewels. Collaboration with H. Schultes, an extraordinary and cooperative psychiatrist with a great ambulance in the beautiful Wachau region in the Danube valley, helped us in this respect, even in a twofold manner. Every Sunday afternoon, one or two of us went 300 km by car first to drink some good Wachauian wine on Sunday night and second to look for untreated, depressed patients in Schultes's ambulance at 7 a.m. on Monday morning. Our group comprised H.-Th. Schröder, doing his thesis; F. Müller, a student; and B. Wasilewski, a friendly young psychiatrist and Alexander von Humboldt fellow from Poland. They did most of the CLO-GH tests. With M. Ackenheil, my former doctoral candidate, and with Hippius, our chief, we often discussed the clinical and laboratory data of the patients.

Since the GH response to CLO was blunted in endogenous depressive patients, but not in nonendogenous depressed patients and controls, we interpreted our results as being evidence of a subsensitivity of postsynaptic α-adrenoceptors or of structures related to them. I presented and intensively discussed our results for the first time at the Sixth World Congress of Psychiatry in Hawaii in September 1977. Ed Sachar, New York, the excellent biological psychiatrist who died too early under tragic circumstances, was chair of this symposium.

About the same time, at the Maudsley Hospital in London, S.A. Checkley[2] came to similar results and conclusions on the basis of his methylamphetamine-cortisol studies and so did G. Laakmann[3] at our hospital with his DMI-GH studies. These studies for the first time gave good evidence for the hypothesis of postsynaptic changes of the α-adrenoceptor sensitivity as a possible neurobiological defect in depression. In the meantime we have learned more about the regulation of α_2-adrenoceptors and GH secretion.[4] Yet, further studies are needed to prove the importance of α-adrenoceptor sensitivity changes in depression. For my research work in depression, I received the following awards: the Anna-Monika-Preis (1971), the Duphar Antidepressant Award (1987), and the Kurt-Schneider-Preis (1988).

1. **Langer G, Heinze G, Reim B & Matussek N.** Reduced growth hormone responses to amphetamine in endogenous depressive patients: studies in normal, reactive and endogenous depressive, schizophrenic, and chronic alcoholic subjects. *Arch. Gen. Psychiat.* 33:1471-5, 1976. (Cited 115 times.)
2. **Checkley S A.** Corticosteroid and growth hormone responses to methylamphetamine in depressive illness. *Psychol. Med.* 9:107-15, 1979. (Cited 60 times.)
3. **Laakmann G.** Beeinflussung der Hypophysenvorderlappen-Hormonsekretion durch Antidepressiva bei gesunden Probanden, neurotisch und endogen depressiven Patienten (Effect of antidepressants on the secretion of pituitary hormones in healthy subjects, neurotic depressive patients, and endogenous depressive patients). *Nervenarzt* 51:725-32, 1980. (Cited 25 times.)
4. **Matussek N.** Catecholamines and mood: neuroendocrine aspects. (Ganten D & Pfaff D, eds.) *Current topics in neuroendocrinology*. Berlin, FRG: Springer-Verlag, 1988. Vol. 8, p. 141-82.

IA-16