Endogenous depressive patients, in comparison to normal controls, nonendogenous, and schizophrenia patients, show a blunted growth hormone response to clonidine. We interpreted our findings as being due to a subsensitivity of postsynaptic a2-adrenoceptors in endogenous depression. [The SCOP and SSCP indicate that this paper has been cited in over 150 publications.]

**a2-Adrenoceptor Subsensitivity in Depression**

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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 noradrenaline 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 Prof. 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. Langcr, a research fellow from Vienna, we found a blunted GH response to amphetamine in endogenous depressive patients in comparison to controls. However, the question whether pre- or postsynaptic disturbances were the main pathophysiological correlate could not be answered. In order to prove a postsynaptic a2-adrenoceptor subsensitivity, we used the recently developed antihypertensive drug, the a2-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 ambition to 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 Wachauer 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 in nonendogenous depressed patients and controls, we interpreted our results as being evidence of a subsensitivity of postsynaptic a-adrenoceptors or of structures related to them. I presented 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 in tragic circumstances, was chair of this symposium.

About the same time, at the Maudsley Hospital in London, S.A. Checkley came to similar results and conclusions on the basis of his methylnaphothamine-cortisol studies and so did G. Laakmann 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 a-adrenoceptor sensitivity as a possible neurobiological defect in depression. In the meantime, we have learned more about the regulation of a2-adrenoceptors and GH secretion. Yet, further studies are needed to prove the importance of a2-adrenoceptor sensitivity changes in depression. For my research work in depression, I received the following awards: the Anna Montika-Price (1971), the Diaphar Antidepressant Award (1987), and the Kurt-Schneider-Preis (1988).


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