

H.M. van Praag, J. Korf, T.P. Kits, F. van Woudenberg, P. Dijkstra, T. Schut (1971). 4-chloor-amphetaminen: toeval en gerichtheid bij de ontwikkeling van nieuwe antidepressiva. *Nederlands Tijdschrift voor Psychiatrie*, 13, 125-141.

#### SUMMARY

The therapeutic effect of antidepressants is customarily related to their ability to enlarge the amounts of functionally active 5-hydroxytryptamine (5-HT) and/or noradrenaline (NA) in the brain. A further evaluation of this hypothesis has become possible with the development of some compounds with a selective effect on the central 5-HT metabolism, namely: p-chloro-N-methylamphetamine (CMA) and p-chloro-amphetamine (4-CA). To begin with, we studied the influence of CMA and 4-CA on the human 5-HT metabolism. On the basis of their biochemical activity, the following predictions were made and tested:

- 1) CMA and 4-CA are antidepressants.
- 2) The antidepressant potency of 4-CA exceeds that of CMA.
- 3) CMA and 4-CA exert little influence on motor activity, and are therefore selective mood improvers.

The first prediction was confirmed; the other two predictions were not. The possible causes of these results are discussed, and avenues of further investigation outlined. It is finally pointed out that the monoamine hypotheses on the mechanism of action of antidepressants make it possible to set a trend for the search for new antidepressants, and to elevate this research above the purely empirical level.