THE GHB-ANALOGUE, GET 73, PREVENTS EITHER THE DEVELOPMENT OF PREFERENCE FOR SUCROSE IN NON-STRESSED RATS, OR THE REDUCTION OF SUCROSE INTAKE IN CHRONICALLY STRESSED RATS

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We have previously shown (1) that the gamma-hydroxybutyrate analogue *N*-(4-trifluoromethylbenzyl)-4-methoxybutanamide (GET 73) inhibits consumption and reinforcing effect of palatable food, in rats. Indeed, it prevents both acquisistion and expression of palatable food-induced conditioned place preference, and reduces the consumption of cafeteria food, at doses that have no detrimental effect on open-field behavior. Here we show that GET 73 is also able to prevent either the development of preference for a sucrose solution in non-stressed rats, or the reduction of preference for a sucrose solution induced by the daily exposure to continuously varied mildly stressful situations (Willner's model of depression).
Methods Adult female Wistar Kyoto rats (180-190 g) were subjected to the Willner's test of depression ("chronic unpredictable mild stress-induced anhedonia"), with some modifications, as described elsewhere. Other rats of the same sex and strain were used to study the development of preference for a sucrose solution.
Results Daily exposure to continuously varied mildly stressful situations produced a reduction of sucrose solution intake starting from the 3rd week, and such reduction became highly significant during the 5th week. Treatment with GET 73 (10, 50 or 100 mg/kg/day, per os) produced a more evident reduction of sucrose solution intake during the 2nd and 3rd week, but during the 4th and 5th weeks the intake dose-dependently increased to values that, for the doses of 50 and 100 mg/kg, were not significantly different from those of non-stressed, vehicle-treated rats. The same doses of GET 73 dose-dependently prevented the development of preference for a sucrose solution in non-stressed rats.
Conclusions The present data indicate that rats treated with GET 73 do not develop the "depression-like" condition produced by the daily exposure, for several weeks, to continuously and unpredictably varied stressful situations, in one of the most valid (face, predictive, and construct validity) "depression" models . Moreover, GET 73 prevents the development of preference for a sucrose solution in non-stressed rats. Concurrently, present and previous data obtained in our and other laboratories suggest that GET 73 "stabilize" the behaviour of rats, either preventing the development of a "depression-like" condition, or of dependence on palatable food (with consequent non-homeostatic, "hedonic" overeating).

(1) Ottani A. et al. Pharmacol Res. 2006 Dec 19