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¹²⁵I-labelled iodothyronines: Useful tools for studies of effects of an antidepressant drug fluoxetine in the rat

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With the use of adapted radiometric enzyme assays for iodothyronine sulfotransferases (ST) and uridine 5'-diphospho-glucuronyltransferase (UDPGT), as well as of our newly developed radiometric assays for iodothyronine deiodinases (IDs) of types 1, 2 and 3 (D1, D2 and D3), we studied the interaction of an antidepressant drug fluoxetine with the metabolism of thyroid hormones (TH) in the rat. TH are supposed to control the activity of some neurotransmitters (e.g., serotonin), which are hypothetically involved in the pathogenesis of depressive illness. One of the pathogenic factors of depression might be inadequate activities of brain IDs that could lead to local insufficient concentration of 3,3',5-triiodo-L-thyronine (T3). This hypothesis led to the development and production of a new group of non-tricyclic antidepressant drugs known as selective serotonine re-uptake inhibitors; fluoxetine is the most frequently used representative of this group.
Effects of subchronic administration (for 25 days) to Wistar rats of fluoxetine by itself, or in combination with T3 were followed. The measurements of ST activities in liver and kidney cytosolic fractions did not demonstrate any significant effects of the administration of fluoxetine, alone or together with T3, on the induction of these enzymes. In contrast, in samples of liver microsomes of rats treated with fluoxetine, we found about two-fold higher UDPGT activities in comparison with control rats.
Even more profound changes in enzyme activities were found in case of IDs, especially in the pituitary and cerebellum. The treatment of rats with fluoxetine alone caused a moderate increase in D2 and, in turn, a slight decrease in D3 activities in cerebellum and some other regions of the CNS. No significant changes in D1 activity were detected. On the other hand, the administration of T3 alone caused, in accordance with our expectation, a substantial decrease in pituitary D2 activity and a simultaneous increase in D1 and D3 activities practically in all tissues studied.

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