Nicotine potentiates imipramine-induced effects on catecholamine metabolism: possible relation to antidepressant activity

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Abstract: Following our behavioral studies demonstrating augmentation of imipramine action by concomitant administration of nicotine, we investigated the effects of one or 14 days of treatment (twice daily) with imipramine and nicotine on dopamine metabolism in various brain areas of rat and noradrenaline in the brain stem. In addition, we evaluated the responses of this metabolism to apomorphine challenge in the mt. Generally, chronic treatment of imipramine and nicotine produced opposite effects to acute administration. As revealed by HPLC, dopamine metabolism in the nucleus accumbens was slightly decreased after 14 days of treatment with imipramine, and co-administration of nicotine resulted in a significant and much more pronounced depression of dopamine metabolism in all investigated dopaminergic structures. Such biochemical effects suggested the development of a compensatory mechanism related with hypersensitivity of dopamine D2 receptors in the mesolimbic and nigrostriatal system. Chronic administration of imipramine produced an opposite effect to the acute one in the brain stem noradrenergic system, like it was observed in dopaminergic structures. Significant inhibition of noradrenaline metabolism after acute administration of imipramine may be explained by its inhibitory effect on noradrenaline reuptake process. In contrast, chronic imipramine administration had no effect on noradrenaline metabolism what indicated the development of sub-sensitivity of α2-adrenoceptors in the brain stem responsible for the role of noradrenaline metabolism. Apomorphine alone decreased metabolism of both catecholamine dopamine and noradrenaline through activation of dopamine D2 receptors which are located also on noradrenergic neurons. The biochemical response to apomorphine in terms of dopamine metabolism was not changed by chronic administration of the investigated drugs but noradrenaline metabolism in the brain stem was strongly attenuated after a combined treatment of imipramine and nicotine. The present data demonstrate facilitation and potentiation of biochemical antidepressant-like effects of imipramine by nicotine co-treatment. We suggest that nicotine may potentiate the antidepressant-like effects of imipramine by promoting some plastic changes in the brain within dopamine and noradrenaline system considerably more strongly than imipramine alone.

Key words: antidepressants, imipramine, nicotine, apomorphine-induced biochemical response, monoamine metabolism in rat brain structures