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Abstract
A comparative study using in vivo microdialysis was conducted to examine the effects of seven amphetamines (methamphetamine, MAP; 3,4-methylenedioxymethamphetamine, MDMA; p-methoxyamphetamine, PMA; p-methoxymethamphetamine, PMMA; 4-methylthioamphetamine, 4-MTA; 3,4,5-trimethoxyamphetamine, TMA; 2,5-dimethoxy-4-iodoamphetamine, DOI) on extracellular levels of serotonin and dopamine. Dialysates were analyzed using HPLC equipped with electrochemical detector following i.p. administration with each drug at a dose of 5 mg/kg. MAP was found to drastically and rapidly increase serotonin and dopamine levels (870% and 1460%, respectively). PMA, PMMA, and 4-MTA slightly increased dopamine levels (150-290%) but remarkably increased serotonin levels (540-900%). In contrast, TMA and DOI caused no detectable changes in levels of both neurotransmitters. We observed that the potent dopamine-releasing activity of MAP was remarkably decreased by introduction of methoxy or methylthio group at the para position (MAP vs. PMMA or 4-MTA), but introduction of two additional adjacent methoxy groups into PMA totally abolished its serotonin-/dopamine-releasing activity (PMA vs. TMA). In addition, para-mono-substituted compounds inhibited both monoamine oxidase (MAO) enzymes more strongly than other compounds; PMA and 4-MTA exhibited submicromolar IC50 values for MAO-A. On the other hand, TMA scarcely affected the activity of both MAO enzymes as well as extracellular levels of serotonin and dopamine. In this comparative study, MDMA, PMA, and 4-MTA functioned similar to PMMA, a typical empathogen. These findings therefore could be helpful in clarifying the psychopharmacological properties of amphetamine-related, empathogenic designer drugs.