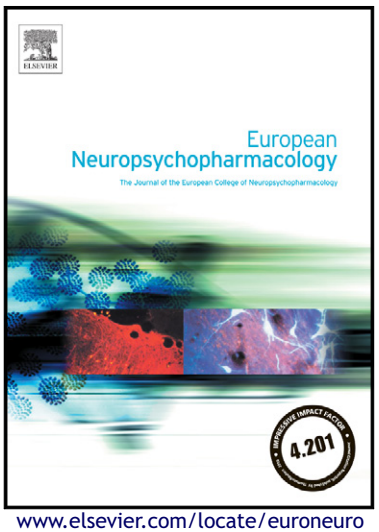


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# 5-Hydroxytryptamine- and Dopamine-Releasing Effects of Ring-Substituted Amphetamines on Rat Brain: A Comparative Study Using *In Vivo* Microdialysis

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**Abstract**

Using *in vivo* microdialysis, a comparative study was conducted to examine the effects of amphetamine-related compounds (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 (5-HT) and dopamine (DA). Dialysates were assayed 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 5-HT and DA levels (870% and 1460%, respectively). PMA, PMMA, and 4-MTA slightly increased DA levels (150–290%) but remarkably increased 5-HT levels (540–900%). In contrast, TMA and DOI caused no detectable changes in levels of both monoamines. We observed that the potent DA-releasing action 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 5-HT-/DA-releasing action (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 $IC_{50}$ values for MAO-A. On the other hand, TMA scarcely affected the activity of both MAO enzymes as well as extracellular levels of 5-HT and DA. 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.