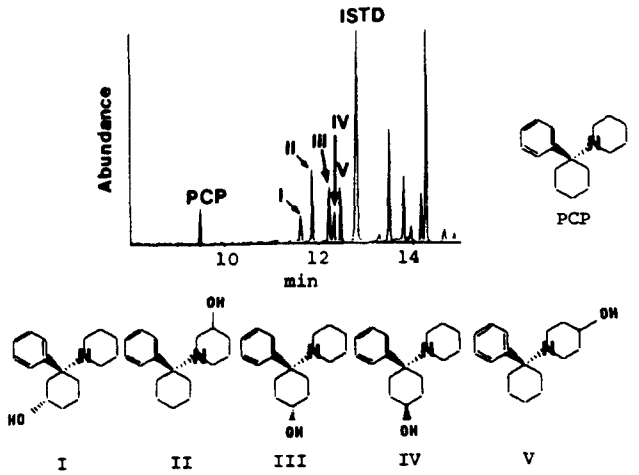
matography-mass spectrometry (GC-MS) procedure was developed to identify PCP, its major metabolites, other PCP analogs and derivatives. The method described is able to separate *m*-OH, *p*-OH, 3-OH pip (II), 4-OH pip PCP (V) and the stereoisomers of 2-OH cyclo, 3-OH cyclo and 4-OH cyclo PCP (III,IV). A sensitive and specific quantitative method was also developed to measure some of these monohydroxy substituted metabolites of PCP from biological samples. The method is based on a two step extraction of PCP related basic metabolites in an organic solvent followed by GC separation and mass selective detection of the extract derivatized with N,O *bis* (trimethylsilyl) trifluoroacetamide. The detection limit of the method was about 5 pmol per injection with a linear standard curve to 3 nmol. The assay was used for the quantitation of monohydroxy metabolites in the urine of PCP-dosed mice and rats. A typical chromatogram of the separation of various PCP metabolites in mice urine is shown below with the labelled peaks identified and remaining peaks unidentified. The 3-CH_2OH pip PCP served as the internal standard (ISTD). The *in vitro* biotransformation of PCP by mouse and rat liver microsomes was also studied. The presence of a recently identified metabolite, *trans* 3-OH cyclo PCP (I), was confirmed. A new metabolite, 3-OH pip PCP (II) was identified and quantitated in the urine and liver microsomal preparations. (Supported in part by NIDA grant DA 1531.)



BINDING STUDIES IDENTIFY TWO CLASSES OF PHENCYCLIDINE (PCP) RECEPTORS IN RAT BRAIN. Haring, R., Y. Kloog and M. Sokolovsky. Laboratory of Neurobiochemistry, Department of Biochemistry, The George S. Wise Faculty of Life Sciences, Tel Aviv University, Tel Aviv 69978, Israel.

Binding experiments were employed in order to differentiate between PCP-receptor sites in rat brain. Two classes of PCP receptors were characterized and localized: one binds [^{3}H]-N-[1-(2-thienyl-cyclohexyl]piperidine ([^{3}H]TCP) with high affinity (K_d=10–15 nM) and the other binds the ligand with a relatively low-affinity (K_d=80–100 nM). The neuroleptic drug haloperidol did not block binding either to the high- or to the low-affinity [^{3}H]TCP sites whereas Ca^{2+} inhibited binding to both. Monovalent ions (K^+ or Na^+) selectively inhibited binding of [^{3}H]TCP or of [^{3}H]PCP to the high affinity sites, via an allosteric mechanism, resulting in the conversion of the high affinity sites to a lower affinity state, which is indistinguishable from the preexisting low affinity site. The two classes of [^{3}H]TCP binding sites have different patterns of distribution. Forebrain regions are characterized by high-affinity sites (hippocampus > frontal cortex > thalamus > olfactory bulb > hypothalamus) but some parts (e.g., hippocampus, hypothalamus) contain low-affinity sites as well. In the cerebellum and in the brainstem only low-affinity sites were detected. Binding sites for [^{3}H]PCP and for its photolabile analog [^{3}H]azido-PCP showed a regional distribution similar to that of the [^{3}H]TCP sites. The results are compatible with the existence of two classes of PCP receptors in the rat brain with a selective localization in the brain. (Supported in part by NIH Grant DABB IR01 DAO4168-01).

ETHYLKETOCYCLAZOCINE (EKC) ANTAGONIZES PHENCYCLIDINE (PCP)-INDUCED STEREOTYPED BEHAVIORS BY REDUCING MONOAMINE RELEASE. Hiramatsu, M., T. Nabeshima, H. Furukawa and T. Kameyama. Department of Chemical Pharmacology and *Department of Medicinal Chemistry, Faculty of Pharmaceutical Sciences, Meijo University, Nagoya 468, Japan.

Administration of PCP to rats induces a complex syndrome of behaviors such as hyperactivity, stereotypy and ataxia and it has been demonstrated that these behaviors are mediated via various neuronal systems. It has been suggested that the psychotomimetic effects of PCP are mediated by PCP/sigma receptors and that the psychotomimetic effects of opiates such as SKF 10,047 also reflect influences of the interaction of PCP/sigma receptors. Tam has suggested that the sedative effect of EKC can mask the observable sigma type behavioral responses. Our purpose in the present study was to investigate whether EKC can affect the PCP-induced stereotyped behaviors in rats. Male Wistar rats (200–300 g) were used. Stereotyped behaviors induced by PCP and SKF 10,047, dopamine-dependent behaviors induced by methamphetamine and apomorphine and serotonin-dependent behaviors induced by *p*-chloroamphetamine and 5-methoxy-N,N-di-methyltryptamine (5-MeODMT) were recorded by the method of Nabeshima *et al.*, Watanabe *et al. and Lee et al.* with some modification, respectively. PCP produced hyperactivity, ataxia and stereotyped behaviors consisting of sniffing, turning, head-weaving and backpedalling. PCP (7.5 mg/kg)-induced stereotyped behaviors were dose-dependently antagonized by EKC (0.25–4 mg/kg). Mr 2266 (2.5 mg/kg), a selective kappa opiate antagonist, antagonized the effect of EKC on PCP-induced stereotyped behaviors. Mr 2266 failed to affect PCP-induced stereotyped behaviors. It is known that PCP-induced stereotyped behaviors are mediated by the dopaminergic and serotonergic neuronal systems. Therefore, we investigated whether EKC affects the dopaminergic and/or serotonergic neuronal systems. EKC antagonized methamphetamine (a dopamine releaser)-induced dopamine-dependent behaviors and *p*-chloroamphetamine (a serotonin releaser)-induced stereotypy, but not apomorphine (a dopamine receptor agonist)-induced dopamine-dependent behaviors and 5-MeODMT (a serotonin receptor agonist)-induced serotonin-dependent behaviors (hind-limb abduction, forepaw treading and Straub tail reaction). These results suggest that EKC, a presumed kappa opioid receptor agonist, antagonized the PCP-induced stereotypy