the United States. In man, PCP produces euphoria, dysphoria, excitation, ataxia, hallucinations and a schizophrenic-like psychosis. Most of the psychotomimetic effects of PCP are believed to be mediated by an interaction with specific PCP receptors. Until recently, it was thought that sigma opioids also interact with PCP receptors to produce dysphoria and hallucinations in man. Using ^{3}H-TCP (1-(1-(2-thienyl) cyclohexyl) piperidine) to label PCP receptors, and ^{3}H-(+)SKF 10,047 (N-allylnormetazocine), a sigma opioid, ^{3}H-haloperidol (in the presence of excess spiroperidol) and ^{3}H-(+)3PPP (N-n-propyl-3-(3-hydroxyphenyl)piperidine) to label sigma opioid binding sites, it was clear that PCP and sigma opioid binding sites were different. The rank order of potencies of several PCP analogs and sigma opioids for inhibiting the binding of ^{3}H-TCP was very different from that for inhibiting the binding of ^{3}H-(+)3PPP, ^{3}H-haloperidol or ^{3}H-(+)SKF 10,047. There were also differences in the anatomical distribution of PCP and sigma opioid binding sites. The physiological relevance of PCP binding sites is supported by the finding that the rank order of potencies for inhibiting the binding of ^{3}H-PCP is the same for inducing ataxia and stereotyped behavior in rats. The sigma opioids, cyclazocine and SKF 10,047, produced PCP-like stereotyped behavior and ataxia, but the sigma opioids also bind to the PCP receptor. Using selective ligands for the PCP, (MK-801) and sigma opioid (rimcazole and 1,3-di-o-tolyl-guanidine) binding sites should help determine the behavioral effects mediated by sigma opioid binding sites. MK-801, which has been reported to be noncompetitive antagonist at N-methyl-D-aspartate (NMDA) receptors, was found to bind potently to the PCP receptor with very little activity at the sigma binding site. In rats, MK-801 produced PCP-like stereotyped behavior and ataxia. PCP-like stereotyped behavior and ataxia was also produced by a competitive antagonist at the NMDA receptor. The (−) isomer of 2-amino-7-phosphonoheptanoate (AP7) was more potent that the racemic AP7 at binding to the NMDA receptor and producing stereotyped behavior and ataxia.

BIOLOGICAL AND CHEMICAL CHARACTERIZATION OF THE ENDOGENOUS ENDOPSYCHOSINS. DiMaggio, D. A., P. C. Contreras and T. L. O'Donohue. Department of Pharmacology, St. Louis, MO, and Division of CNS Research, Searle/Monsanto, St. Louis, MO.

Previous reports from our lab have demonstrated the existence of endogenous ligands for the phencyclidine (PCP) and the *sigma* receptors. The existence of two separate ligands supports previous data which indicate that the two receptors are distinct both in pharmacology and distribution. These endogenous ligands, which were isolated from preparative scale porcine brain acid extracts, have been designated *alpha-* and *beta*-endopsychosin. *Alpha*-endopsychosin inhibited the binding of ^{3}H-PCP to rat brain membranes in a selective and dose dependent manner, while *beta* endopsychosin selectively and specifically inhibited binding of ^{3}H-SKF 10,047 (N-allylnormetazocine), a sigma opioid, to rat brain membranes. The endopsychosins each have a distinct distribution in the CNS. Biological and chemical characteristics of the two ligands will be compared. Work done with antibodies generated against a sequenced portion of the beta ligand will be presented.

PCP AND ANALOGS SUPPRESS T LYMPHOCYTE PROLIFERATION BY PREVENTING THE MITOGEN-TRIGGERED RISE OF FREE CYTOSOLIC CALCIUM CONCENTRATION, A MESSAGE REQUIRED FOR IL-2 SYNTHESIS. Dornand, J., J. M. Kamenka* and J. C. Mani. CNRS ER228 and *CNRS LP8402, INSERM U249, ENSCM, Montpellier, France.

The psychotomimetic drug PCP displays a vast array of known pharmacological effects, among them is its capacity to affect cation transport in nervous and myocardiac tissues. Since increased movements of cations are essential for the immune responses, it has been mentioned that PCP and its analogue ketamine used for general anesthesia could also depress immune functions by this mechanism. In order to check this hypothesis, we have investigated the effects of PCP and of many other structural derivatives on the blastogenic response of murine or human T lymphocytes to mitogenic lectins. We find that, except ketamine, all the drugs we tested block an early event of T lymphocyte activation and prevent their further proliferation; conversely, when added later after the mitogen, they do not affect primed lymphocytes; in the same way they do not inhibit the IL-2 dependent proliferation of the cytotoxic T cell line. The inhibitory action of the drugs can be reversed by extensive washings of the cells. At concentrations preventing lymphocyte blastogenesis, PCP and its derivatives do not inhibit interleukin-1 (IL-1) production from LPS-stimulated macrophages, which suggests that these cells are not the target of the drugs. Conversely, they lower interleukin-2 synthesis from activated T helper cells. The inhibition of IL-2 production paralleled that of lymphocyte proliferation. The negative action of all the drugs appears to be related to the inhibition of the rise of $[Ca^{++}]_i$ (free cytosolic calcium concentration) observed soon after the T receptor triggering and which is an essential message for IL-2 production. Lymphocyte membrane depolarization induced by the drugs could explain the blockade of the lectin-induced $[Ca^{++}]_i$ changes. The study of the structure-activity relationship shows that the PCP analogs which possess a quasi-rigid conformational structure express an inhibitory capacity of the T lymphocyte proliferation higher than that of PCP (200 times for some products). Since these compounds poorly interact with the CNS tissues and have few comportmental effects, we suggest that PCP exerts its negative action in lymphocytes on biochemical entities different from its receptor(s) in the CNS; this could explain that ketamine has no action on lymphocyte mitogenesis.

EFFECTS OF DRUGS ON PHENCYCLIDINE STIMULATED LOCOMOTION AND ATAXIA IN MICE. Downs, D. A., J. N. Wiley and R. J. Labay. Department of Pharmacology, Warner-Lambert/Parke-Davis, Ann Arbor, MI 48105.

Phencyclidine caused dose-related increases in explora-