though to a much lesser extent, (d) the propargyl derivative, (*4*, R=CH=CH_2–) seems to evoke in monkeys a "hallucinogenic effect" similar to that of phencyclidine.

EFFECTS OF SELECTIVE CORTICAL AND SUBCORTICAL LESIONS ON TCP AND NMDA RECEPTOR BINDING. Maragos, W. F., D. C. M. Chu, A. B. Young and J. B. Penney. Department of Neurology, University of Michigan, Ann Arbor, MI 48104.

The dissociative anesthetics (phencyclidine, ketamine, and N-(1-[2-thienyl]cyclohexyl])-piperidine (TCP) are a unique class of drugs which appear to interact with a site closely linked to the channel of the N-methyl-D-aspartate (NMDA) receptor. While much data has recently been gathered concerning the pharmacological, electrophysiological and behavioral interactions between these two sites, little is known about their neuronal localization. We have studied both sites autoradiographically in serial sections of rat brains after specific lesions. Male Sprague-Dawley rats (200 g) were anesthetized and lesioned in the (1) nucleus basalis using ibotenate, (2) cerebral cortex using ibotenate, (3) entorhinal cortex using knife cuts and (4) dentate gyrus using colchicine. After one week, animals were decapitated, the brains frozen and samples taken for CAT activity and histological examination. Serial sections were assayed for TCP and NMDA receptors using [3H]TCP and [3H]glutamate as previously described (Maragos *et al.*, *Eur J Pharmacol* **123**: 173–174, 1986). After nucleus basalis lesions neither binding site was altered in cortex. Entorhinal knife cuts resulted in only a 9% decrease in dentate TCP binding. Cortex and dentate lesions caused local 94–98% and 84–92% reductions in both receptor sites, respectively. The data suggest that NMDA and TCP receptors have similar localizations and that for the most part, they are localized postsynaptically. (Supported by USPHS grants AG 06155 and NS19613 and the ADRDA.)

KETAMINE PREVENTS GLUTAMATE-INDUCED CALCIUM INFLUX AND ISCHEMIC NERVE CELL INJURY. Marcoux, F. W., J. E. Goodrich, A. W. Probert, Jr. and M. A. Dominick. Departments of Pharmacology and Toxicology and Experimental Pathology, Warner-Lambert/Parke-Davis Pharmaceutical Research, Ann Arbor, MI 48105.

Ketamine has been reported to block glutamate and hypoxia-induced neuronal injury in culture. Glutamate's excitotoxic effects have been proposed to be the result of intracellular calcium accumulation via NMDA receptor-coupled channels. We examined the effects of ketamine against glutamate-induced calcium influx into cultured neurons from the rat cerebral cortex and against ischemic neuronal injury in vivo in the gerbil hippocampus. Cells were harvested from neonatal cerebral cortex, cultured in 96-well plates (2×10^5 cells per cm^2) for 8–14 days, preincubated for 30 min in $^{45}C^{++}$ and then challenged for 30 min with 100 μM glutamate with or without (+)-ketamine. After wash, intracellular $^{45}Ca^{++}$ concentration was measured for individual wells in a scintillation counter. Ketamine's effect on ischemic CA1 neuronal injury were assessed using a temporary bilateral carotid occlusion model in gerbils. The effects of Ketalar®(ketamine hydrochloride) pretreatments were assessed on global ischemia-induced increases in exploratory locomotor activity and depletion of hippocampal pyramidal neurons. One hundred μM glutamate-induced $^{45}Ca^{++}$ influx into cultured neurons was assessed on control wells and in the presence of ketamine at 0.001 to 1000 μM concentrations. At 250 μM, ketamine inhibited glutamate-induced $^{45}Ca^{++}$ influx by 90%; the IC_{50} was 6.8 μM. Gerbils were administered 100, 150 or 200 mg/kg Ketalar® pretreatments 30 min before 10 min of bilateral carotid occlusion. Exploratory locomotor activity 24 hr later and CA1 hippocampal light microscopic histopathology 2 weeks later were compared with that of vehicle pretreated control gerbils. There were dose-related attenuations in the hyperlocomotor activity responses of the Ketalar® vs. control gerbils; the anesthetic 200 mg/kg Ketalar® dose prevented an increase in locomotor activity. In the same Ketalar® vs. control gerbils there were dose-related reductions in CA1 neuronal depletion as judged by a blinded histopathological evaluation. Five out of 12 gerbils given the 200 mg/kg Ketalar® pretreatment showed no CA1 neuronal depletion. These results support a glutamate antagonist action for ketamine. In addition, the findings with gerbils suggest that Ketalar® anesthesia protects against ischemic neuronal injury. Further studies may provide evidence that ketamine's inhibition of glutamate-induced calcium influx is responsible for its apparent neuroprotective action as shown by the present results.

PRIMARY CULTURE OF MONOAMINERGIC NEURONS AS A MODEL OF THE SCREENING OF PCP DERIVATIVES. Marlier, L., M. J. Drian, J. M. Kamenka* and A. Privat. Neurobiologie du developpement, INSERM U-249, CNRS LP 8402 and *Laboratoire de Biochimie Générale ENSCM Montpellier, France.

The brainstem of 13–14 days rat foetuses was dissected in order to prepare cell suspensions containing either serotonergic or dopaminergic or noradrenergic neurons. These suspensions were plated on multiwell dishes coated with polylysin and cultivated in a semi-synthetic medium for periods up to two weeks. Monoaminergic neurons were immunocytochemically identified with specific antibodies against serotonin, dopamine and noradrenaline. Specific uptake of the corresponding neurotransmitters was controlled with radioautography, and found to coincide with immunocytochemical label. The ability of a new PCP derivative, GK 13, to inhibit specific uptake of monoamines was assayed on the three culture models. It was found that the drug inhibited 50% of the uptake at a concentration of 0.7 10^{-6} M for serotonin, 0.1 10^{-6} M for dopamine and noradrenaline. Moreover, when compared with nomifensin, GK 13 was found much more potent as an inhibitor of dopamine uptake. These results will be compared with those obtained with PCP and other derivatives. These data suggest that primary cultures of identified monoaminergic neurons are a useful tool for the study of the characteristics of PCP and its derivatives. (Supported by INSERM and CNRS.)