311.13 CORTICAL LESIONS DECREASE BASAL AND AMPHETAMINE-INDUCED RELEASE OF ASCORBATE IN THE NEOSTRIATUM. Allison Basse-Tomusk and George V. Rebec. Dept. Psychol., Indiana Univ., Bloomington, IN 47405

The neostriatum contains very high levels of extracellular ascorbate (AA) that show marked circadian (O'Neill et al. (Neurosci. Lett, 42:105, 1983) and drug-induced changes (Kamata et al. Brain Res. 362:331, 1986). However, the source or sources of neostriatal AA release are unknown. O'Neill et al. (1983) have suggested that basal extracellular AA levels in the neostriatum are regulated by the corticostriate pathway since cortical lesions decrease extracellular AA levels by 80%. In the present experiment, we sought to determine whether the corticostriate pathway also is involved in amphetamine-induced AA release.

Adult, male rats received bilateral-suction lesions of the dorsal aspect of the neocortex from 1mm posterior to bregma to the frontal pole. Another group of animals received sham lesions in which only the dura was removed. Following an 8 to 10 day recovery period, basal and amphetamine-induced (2.0 mg/kg, i.v.) AA release were assessed with in vivo voltammetry using electrochemically-modified carbon fiber electrodes. These electrodes provide a voltammetric wave for AA that is resolved easily from that for catechols and all other electroactive species in the mammalian brain. Voltammetric scans, obtained at 2-min intervals, were displayed in a differential form.

Consistent with previous reports, cortical lesions decreased basal levels of AA by 80%. Furthermore, amphetamine-induced AA release also was reduced dramatically. These results suggest that the corticostriatal pathway plays a crucial role in the neuromodulatory actions of neostriatal AA.

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311.14 HALLUCINOGENS BIND TO COMMON RECEPTORS IN THE RAT FOREBRAIN: A COMPARATIVE STUDY USING ^{125}I-LSD AND ^{125}I-DOI, A NEW PSYCHOTOMIMETIC RADIOLIGAND. D. J. McKenna*[1], C. A. Mathis*[2], A. T. Shulgin*[2], & J. M. Saavedra[1] (SPON: N. Buckholtz). 1. Section on Clinical Pharmacology, Laboratory of Clinical Science, NIMH, Bethesda, MD 20892 2. Donner Laboratory, Lawrence Berkeley Laboratory, University of California, Berkeley, CA 94720.

Autoradiographic methods were applied to the characterization of hallucinogen-specific receptors using two 5HT$_2$ specific ligands, ^{125}I-LSD, and a new psychotomimetic radioligand, [^{125}I]-4-iodo-2,5-dimethoxyphenylisopropylamine (^{125}I-DOI). The R(-) and S(+) enantiomers of ^{125}I-DOI were synthesized to radiochemical purity at a specific activity of 1700 Ci/mmol and 1200 Ci/mmol, respectively. In rat cortical homogenates R(-)-[^{125}I]-DOI showed saturable, specific binding (Kd: 1.41 nM, Bmax: .112 pmol/mg protein, one site model). Sixteen micron rat forebrain sections incubated in 200 pM concentrations of each enantiomer showed high densities of specific binding in the cortex (layer IV), claustrum, lateral olfactory tracts, nucleus acumbens, and diagonal band. Both enantiomers were completely displaced from all sites by unlabelled DOI and unlabelled LSD (1 uM). Sections incubated with ^{125}I-LSD under identical conditions showed a similar pattern of regional specific binding. ^{125}I-LSD also showed specific binding in the caudate-putamen, while ^{125}I-DOI showed virtually no specific localization in this region. Incubation of 200 pM ^{125}I-LSD or the ^{125}I-DOI enantiomers in the presence of various hallucinogens and hallucinogen analogs (500 nM) showed selective, regional displacement. ^{125}I-LSD was specifically displaced from the claustrum and cortex, but not from the caudate, nucleus acumbens, or olfactory tracts, by both enantiomers of DOI and DOB, but not by the inactive analog alpha-ethyl DOM. The tryptamine hallucinogens DMT and 5-MeO-DMT at 500 nM partially displaced ^{125}I-LSD. ^{125}I-DOI showed a similar displacement pattern in the presence of these unlabelled ligands. The displacement of two psychotomimetic radioligands from binding sites in the claustrum and cortex by members of each structural class of hallucinogens provides evidence that indole, ergoline, and phenylisopropylamine hallucinogens act at common receptors located in these brain regions.

311.15 COLOCALIZATION OF TRANSMITTER BINDING SITES ON THE LEVEL OF HIPPOCAMPAL LAYERS IN THE RAT AND HUMAN BRAIN. K. Zilles*, A.Schleicher, E.Horvath, D.Spencer. Anatomical Institute, University of Köln, 5000 Köln 41 and Troponwerke, 5000 Köln 80, FRG.

Information processing in the hippocampus depends on the action of many different transmitters. As a first step, to analyze possible interactions, the correlation in regional distribution of receptors for the classical transmitters acetylcholine (ACh), glutamate (Glu), GABA and serotonin (5-HT) was studied in all regions and layers of the rat and human hippocampus on frozen sections (20µm) with quantitative receptor autoradiography. The muscarinic ACh receptors were labelled with (3H)N-methyl-scopolamine(0.2nM), the M1 subtype with (3H)pirenzepine (5-10nM), The M2 subtype with (3H)oxotremorine-M, the Glu receptors with (3H)L-glutamate (100nM) both in presence or absence of Ca^{++}/Cl^{-}, the GABA receptors with (3H)muscimol (5-10nM), the 5-HT1 receptors with (3H)5-HT (2.5nM), and the 5-HT1A subtype with (3H)ipsapirone (5nM). Specific binding was measured in presence of the respective unlabelled compounds with an image analyzer (Zilles,K. et al., J.Neurosci.Meth., 18:207,1986).

The comparison of the quantitative distribution pattern of the actual binding sites with the immunohistochemically identified axonal terminals shows a clear mismatch in all cases, which suggests a different regulation of transmitters and their receptors. The comparison between the distribution in rat and man shows a high similarity in the Glu receptors, but no concordance in 5-HT receptors, which indicates caution in generalizing the rat model. The most important result is the colocalization of some, but not all of these receptors on the level of hippocampal layers. High correlations between the distributional pattern of 5-HT1A receptors on one side and M1 or Glu receptors on the other side, as well as between M1 and Glu receptors have been found. This can be an argument for interactions of different receptors in the same layer, which has already been demonstrated for Glu and α_1-adrenoreceptors (Nicoletti,F. et al., Proc. Natl.Acad.Sci.USA, 83:1931,1986).

311.16 NEURONS IN THE ROSTRAL VENTROLATERAL MEDULLA OBLONGATA CONTAIN MULTIPLE MESSENGERS. D.E. Millhorn, T. Hökfelt and K. Seroogy. Dept. of Physiology, University of North Carolina, Chapel Hill, N.C. 27514 and Dept. of Histology, Karolinska Institute, Stockholm, Sweden.

Although it is generally accepted that neuronal networks in the ventrolateral aspect of the medulla oblongata play an essential role in control of the respiratory and cardiovascular systems, relatively little is known about the chemical nature of cells in this region of the brainstem. The present study was devoted to identifying coexistence patterns of neurotransmitters and peptides in a region of the ventrolateral medulla that corresponds anatomically to nucleus paragigantocellularis (PGL).

Adult rats were pretreated with colchicine 24-48 hr prior to transcardial perfusion with a mixture of picric acid and formalin. Sections were cut on a cryostat (14µm) and processed for an indirect immunofluorescence technique that allowed simultaneous identification of multiple chemical messengers in individual cells. In some instances Fluoro-Gold (FG), a retrograde transported dye, was injected into either the nucleus tractus solitarii (NTS) or spinal cord 7 days prior to colchicine pretreatment.

Three types of coexistence (transmitter-transmitter, transmitter-peptide and peptide-peptide) were found. For example, a substantial number of individual cells in PGL stained positive for the classical transmitters serotonin (5-HT) and GABA. Moreover, a number of 5-HT/GABA cells were labelled with FG that had been injected into the thoracic spinal cord. We also found that 5-HT in the region of PGL coexists with several peptides including enkephalin (ENK) and cholecystokinin (CCK). The type of coexistence most often encountered involved the peptides somatostatin (SOM) and ENK. Numerous perikarya that showed positive immunostaining for both SOM and ENK were found at all rostral-caudal levels of PGL. Furthermore, a substantial proportion of the SOM/ENK cells were labelled with FG that had been injected into either NTS or the spinal cord. Finally, we found that essentially all 5-HT somata in PGL and caudal raphe complex as well as the epinephrine-containing cells in the C1 area of the ventrolateral medulla showed positive immunostaining for acetylcholinesterase. (Supported by Swedish MRC grant 04X-2887 and NIH grant HL 33831).