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Comparison of Tranylcypromine- and Phenelzine-Induced Changes in Trace Amine Levels in Brain and Urine. D.F. LeGatt*, G.B. Baker*, R.T. Coutts* and J.M. Baker* (Spon: G.B. Frank). Neurochemical Research Unit, University of Alberta, Edmonton, Alberta, Canada T6G 2G3

Trace amines have been implicated in the etiology of various nervous disorders and in the actions of drugs utilized in the treatment of such disorders. The effects of two antidepressants, the monoamine oxidase (MAO) inhibitors phenelzine (PLZ) and tranylcypromine (TCP), on brain and urine levels of 2-phenylethylamine (PEA), para-tyramine (p-TA), and tryptamine (T) were investigated in separate groups of rats administered the drugs i.p. once daily (10 mg/kg for TCP and 15 mg/kg for PLZ) for 1, 2, 8, and 19 days. Rats were sacrificed 6 h after the final dose. Analyses of T, PEA, and p-TA were based on procedures utilizing electron-capture gas chromatography with capillary columns (Calverley et al., Can. J. Neurol. Sci., 7, 237 (1980); Baker et al., Biochem. Soc. Trans., in press). Brain levels of PEA and T were several times higher with TCP than with PLZ for all time periods except for day 19, when PEA levels with PLZ had attained those found with TCP. For p-TA, brain levels peaked above control after 2 days and declined thereafter with TCP, but progressively increased to day 18 with PLZ. These differences between the two drugs may be due to factors other than inhibition of MAO since both drugs caused greater than 90% inhibition of MAO by day 2. A correlation between brain and urine levels was demonstrated. (Supported by MRC of Canada)

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DOPAMINE- AND SEROTONIN-SENSITIVE ADENYLATE CYCLASE IN THE GILL OF *APLYSIA*. Sam Weiss* and George I. Drummond. University Biochemistry Group, University of Calgary, Calgary, T2N 1N4 Canada.

Stimulation of adenylate cyclase by dopamine (DA) and serotonin (5-HT) was examined in 38,000 x g pellets from *Aplysia* gill homogenates. DA stimulated enzyme activity 3 to 5-fold over basal (EC_{50},10μM), 5-HT stimulated 15 to 20-fold (EC_{50}, 1μM). Several ergot alkaloids were also effective. LSD-25 acted as a partial agonist (efficacy 0.45, EC_{50},2μM), ergotamine was equieffective to 5-HT but 10 times more potent (EC_{50},0.1μM). At subsaturating concentrations of 5-HT (10nM to 1μM), DA (5μM) further augmented enzyme activity; at saturating concentrations of 5-HT (10-100μM), DA produced no additional stimulation. Activation by structural analogs of DA and 5-HT provided evidence for similar structural requirements for both agonists. Stimulation by DA, 5-HT and ergotamine was antagonized by the 5-HT antagonists 2-bromo-LSD, methergoline, and cyproheptadine and also by the DA antagonists chlorpromazine and haloperidol. Stimulation by ergotamine in the presence of 50μM chlorpromazine or methergoline resulted in a rightward-shifted two component dose-response curve. The first component (EC_{50},0.5μM) accounted for 75% of total stimulation by ergotamine, the second component (EC_{50},25μM) accounted for the remainder. These findings suggest that structural similarities exist between the receptors that mediate DA and 5-HT stimulation of adenylate cyclase. Saturating concentrations of 5-HT or ergotamine may fully activate both DA and 5-HT receptors resulting in maximum activation of the enzyme. (Supported by MRC of Canada).

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POSTSYNAPTIC ACTIVITY OF PROSTAGLANDINS AS SHOWN BY THE INHIBITION OF APOMORPHINE-INDUCED CIRCLING IN MICE. R. D. Schwarz,* N. J. Uretsky, J. R. Bianchine. Ohio State University, Dept. of Pharmacology, Colleges of Medicine and Pharmacy, Columbus, OH 43210.

We have recently shown that prostaglandins (PGs) are able to inhibit amphetamine-induced circling. In order to determine whether PGs are acting at postsynaptic sites, we have tested the ability of PGs to inhibit circling produced by apomorphine, a direct dopamine (DA) receptor agonist. Male mice were electrolytically lesioned (2.5 ma/20 sec) in the left striatum and allowed 4 days to recover. On the day of testing the mice were injected in the right striatum with either PG or saline followed 10 min later by apomorphine (1 mg/kg; i.p.). Total ipsilateral turns were counted at 5 min intervals over a period of 15 min. PGE_2, PGD_2 and $PGF_{2\alpha}$ all inhibited circling at a dose of 1.0 μg. Both PGE_2 and PGD_2 blocked circling at 0.3 μg, while only PGE_2 inhibited circling at 0.1 μg. The PGE_2 metabolite (13,14-dihydro-15 keto PGE_2) was ineffective at 1.0 μg. This observation as well as the differential potency of the PGs suggests that the inhibition of circling was not due to nonspecific effects. PG administration alone did not alter circling when compared to that produced by saline control. Thus, these results extend our previous observations that PGs are active in the CNS, and are able to inhibit a DA-mediated behavior. More importantly, these results suggest a postsynaptic site of action for PGs within the DA system. (Supported in part by NS 13888.)

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DESIPRAMINE RELEASES ENDOGENOUS DOPAMINE FROM RAT HYPOTHALAMUS BUT NOT STRIATUM. Richard E. Tessel and Sharie L. Myers*, Univ. of Kan., Lawrence, KS 66045

Dopamine (DA) nerve terminals in rat corpus striatum (CS) differ from those within the hypothalamus (HT) both biochemically and pharmacologically (Moore et al., Fed. Proc. 39, 2912, 1980). To determine if desipramine (DMI)-norepinephrine (NE) and -DA interactions are also tissue selective, we evaluated the effects of a 30 min in vitro incubation (37°C) of CS and HT with DMI on the overflow of endogenous catecholamines. NE, DA and epinephrine (EPI) were determined simultaneously using HPLC with electrochemical detection. DMI significantly increased NE and DA overflow from HT at a concentration as low as 10^{-8}M; increased overflow of HT EPI required 10^{-5}M DMI. Additionally, the drug did not increase the overflow of striatal DA or NE until the DMI concentration reached 10^{-4}M. The data support the idea that striatal DA neurons are not representative of all DA neurons, extends this concept to NE neurons, and suggests that DA may be involved in the effects of antidepressant therapy. [Supported by Grants from ADAMHA (DA 01614) and NIH (HL 24093)]

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CONDITIONS DISTINGUISHING BETWEEN ALTERED NEURONAL ENTRY RATE AND PERIPHERAL DISPOSAL IN RAT SERUM DOPAMINE-*beta*-HYDROXYLASE (DBH) ACTIVITY REGULATION. Jeffrey H. Hurst*, Bruce C. Nisula* and Jon M. Stolk, Maryland Psychiatric Research Center, Univ. of Maryland School of Medicine, Baltimore, MD 21228 and Developmental Endocrinology Branch, NICHD, NIH, Bethesda, MD 20205.

DBH enters the circulatory compartment from sympathetic neurons. Alterations in either the DBH entry rate into the circulation or the DBH metabolic clearance rate can alter serum DBH activity. Our previous work demonstrated that increased rat serum DBH activity (in hypothyroidism, diabetes) could be accounted for by reductions in DBH disposal. We sought to define a condition in which altered serum DBH activity was effected by altered enzyme entry rates. Our hypothesis was that thyroxine (T4) and 6-hydroxydopamine (6OHDA) both decrease serum DBH activity, but by different mechanisms. Treatment of F344 female rats with 100 ug T4/kg for 2 wk caused a 35% decrease in serum DBH activity; the initial half-time of DBH disappearance after bolus injection was shortened after T4 (11.6 min vs. 20.0 min in controls). In contrast, the 24% decrease in serum DBH activity after 6OHDA was not associated with an altered initial half-time of disappearance (18.2 vs. 18.8 min in controls). These findings suggest that T4 lowers serum DBH activity by increasing DBH disposal, whereas 6OHDA lowers serum DBH activity by decreasing neuronal DBH entry rate. The results with 6OHDA provide the first metabolic evidence in intact rats for changes in serum DBH activity due to parallel changes in DBH release from neurons. (Supported by USPHS MH 32842).

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MEASUREMENT OF DOPAMINE CONTENT AND BIOSYNTHESIS IN THE RAT RETINA, IN VITRO. L. S. Pittman* J. Donnelly* W. K. O'Steen and D. K. Sundberg. Bowman Gray School of Medicine, Winston-Salem, N.C., 27103

The amocrine cells of the retina possess a dopaminergic system which has been shown to be activated by light. In this report we have applied a recently developed technique for concurrently monitoring dopamine (DA) content and synthesis in the rat retina, in vitro. (Sundberg et al., Res. Comm. Chem. Pathol. Pharmacol. 29, 1980). Retinas are rapidly dissected from the eye and incubated in Earles salt solution containing 5uCi. of ^{3}H-tyrosine. After incubation, the retinas are extracted in methanol and the amines purified by alumina absorption. DA is separated by reverse phase chromatography, measured by amperometric detection and the tritiated fractions counted to determine synthetic rates. Retinas incubated for 15, 30, and 60 min. show a linear incorporation of ^{3}H-tyrosine, reaching 205 dpms at one hour. This was associated with a decrease in DA content from 27 to 15 pg/mg. DA synthesis in retinas from animals having hereditary retinopathy or light induced destruction of photoreceptors were not significantly different from controls. This technique should provide a useful tool for investigating aminergic modulation of visual function.

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