STRATEGIES FOR ENHANCING CATECHOLAMINE-MEDIATED NEUROTRANSMISSION

(NASA Grant NAG 2-210; Previous title: Effects of Tyrosine or Melatonin on Brain Function and Behavior)

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Major findings made during this project period included the observations that:

a) changes in tyrosine availability do affect brain dopamine release, as assessed by in vivo microdialysis, but that neuronal feedback mechanisms limit the durations of this effect except when dopaminergic neurotransmission has been deficient;

b) the circulating hormone TRH markedly stimulates brain dopamine release, an effect probably mediated by its diketopiperazine metabolite;

c) the amount of circulating L-dopa which enters the brain is both enhanced by carbohydrate consumption and suppressed by protein intake; both nutritional effects can be damaging, inasmuch as a sudden rush of L-dopa into the brain can facilitate dyskinesias, while the inhibition of brain L-dopa uptake by proteins suppresses its conversion to brain dopamine; an appropriate mixture of diet, proteins and carbohydrates can obviate both effects;

d) serotonin release from superfused hypothalamic slices is a linear function of available tryptophan levels throughout the normal dynamic range;

e) the daily rhythm in plasma melatonin levels is abnormal both in the Sudden Infant Death Syndrome and in women with Secondary Amenorrhea;

f) tyrosine can potentiate the anorectic effects of widely-used sympathomimetic drugs;

g) newly-described COMT inhibitors can enhance brain dopamine release in vivo;

h) a cell culture system, based on Y-79 (retinoblastoma) cells exists, in which melatonin reliably suppresses dopamine release.

C1. PUBLICATIONS BASED ON RESEARCH SUPPORTED BY NAG 2-210 (1988-1992)

I. CATECHOLAMINES, TYROSINE

Acworth, I.N. and Wurtman, R.J.

Acworth, I.N. and Wurtman, R.J.

Berry, E.M., Growdon, J.G., Wurtman, J.J., Caballero, B., and Wurtman, R.J.
Caballero, B., Gleason, R.E., and Wurtman, R. J.  

During, M.J., Acworth, I.N., and Wurtman, R.J.  

During, M.J., Acworth, I.N., and Wurtman, R.J.  

Kreutz, M.R., Acworth, I.N., Lehnert, H., and Wurtman, R.J.  

Lehnert, H. Beyer, J., Reinstein, D.K., Richardson, U.I., and Wurtman, R.J.  

Milner, J.D. and Wurtman, R.J.  

Wurtman, R.J., Caballero, B., and Salzman, E.  

II. EXERCISE EFFECTS

Conlay, LA., Maher, T.J., and Wurtman, R.J.  

Conlay, L., Wurtman, R.J., Maher, T.J., Lopez G.-C., I., Blusztajn, J.K., Vacanti, C.A., Logue, M., During, M., Caballero, B., and Evoniuk, G.  

Wurtman, R.J. and Lewis, M.C.  
III. SEROTONIN, TRYPTOPHAN

Gardier, A. and Wurtman, R.J.

Caballero, B. and Wurtman, R.J.


Schaechter, J.D. and Wurtman, R.J.

Schaechter, J.D. and Wurtman, R.J.

Schaechter, J. and Wurtman, R.J.

IV. MELATONIN

Brzezinski, A. and Wurtman R.J


Deng, M.H., Lopez G.-Coviella, I., Lynch, H., and Wurtman, R.J.


Wurtman, R.J. and Lieberman, H.R.

V. RELATED REVIEW ARTICLES

Wurtman, R.J.

Wurtman, R.J.

Wurtman, R.J.

Wurtman, R.J.