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Prograss Report for AFOSR/AASERT 2/16/94

Toda C. Holmes. Ph.D., Fellowship Recipient

The offices of lesion of ascending modulatory transmitter systems on phospholipid metabolism in the rat brain: models for neurotransmitter regulation of phospholipid metabolism.

My thesis research in Dr. Richard Wurtman's laboratory centered on the interactions between acetylcholine and phospholipid metabolism, specifically, on changes of phospholipid metabolism and mass in cortical terminal fields after removal of cholinergic innervation. Before receiving the AASERT fellowship, I found that phospholipid and phospholipid metabolite levels in frontoparietal cortex are decreased following excitotoxic lesion of the basal for abrain cholinergic nucleus basalis (nBM). nBM lesions were verified by the measurement of choline acetyltransferase activity and evoked acetylcholine release in cortical slices.

After receiving the AASERT fellowship, I conducted post-nBM lesion tigecourse studies in order to determine whether cholinergic and phospholipid metabolism recovers after unilateral lesions. Choline acetyltransferase activity and evoked acetylcholine release in cortical slices showed an eventual recovery after the lesion. The decreases in cortical phospholipids also recovered after the lesion, the time course was similar to that seen for evoked acetylcholine release. Cholinergic lesion by surgical sectioning resulted in decreased cortical phospholipids, also while excitotoxic lesions of non-cholinergic projections to cortex did not change phospholipid levels. Radiolabelling and enzyme assay experiments with cortical tissues indicate that phospholipid biosynthesis is decreased following nBM lesion. This decrease occurs at the point of choline kinase. Phospholipid turnover in cortex may also be increased following nBM lesions, as indicated by muscarinic inositol lipid hydrolysis and choline radiolabelling of cortical tissues, dhal-

In conclusion, cortical phospholipid biosynthesis and hydrolysis is altered following loss of cholinergic input.

