

CHOLINERGIC-MONOAMINERGIC INTERACTIONS IN SELECTED REGIONS OF THE
BRAIN: HISTOCHEMICAL AND PHARMACOLOGIC ANALYSES

L.L. Butcher*,**, N.J. Woolf**, A. Albanese* and
S.H. Butcher***

*Department of Psychology
**Brain Research Institute, and
***Mental Retardation Research Center
University of California, Los Angeles, California 90024

INTRODUCTION

The elucidation of neuronal circuitry has been a major goal in the neurosciences. Anatomic studies with radioactive amino acids and other neuronally transported substances such as horseradish peroxidase have focussed on possible relationships among different cell body groups in the central nervous system. In most of these experiments, however, neurochemical features of the relevant neural regions are usually not considered. Yet immense interest in certain of these neurochemicals exists, especially transmitters and related substances involved in neuronal communication processes, because of their obvious or apparent significance for functional neurobiology. In the present report we attempt to address the problem of transmitter neuroanatomy in three regions of the brain thought to be involved in cholinergic-monoaminergic interactions: the substantia nigra, corpus striatum and locus ceruleus.

Distribution of Cholinergic Substances in the Brain:
Histochemical Studies

Histochemical studies of cholinergic substances in the brain have been restricted almost entirely to four neurochemical entities (6): choline-O-acetyltransferase (CAT, EC 2.3.1.6), acetylcholin-

esterase (AChE, EC 3.1.1.7) and muscarinic and nicotinic receptors. Of these, morphologic detail has been best elucidated for the synthetic and degradative enzymes and, accordingly, it is to these two substances that the remainder of this discussion is directed.

CAT: Controversy exists concerning the reliability and validity of currently available histochemical methods for CAT (6). Although the lead-trapping protocol for the enzyme has long ceased to be a viable histochemical technique (see 6), immunohistochemical methods are being pursued vigorously but not without their difficulties (6). As pointed out by Rossier (38), a major concern has been the purification of CAT and the specificity of the antibodies directed against the enzyme. Hattori and his associates (21,22), for example, initially described the association of CAT with medium sized spiny neurons in the caudate-putamen complex. In a more recent report from the same laboratory, however, Kimura et al. (23), using a newly purified enzyme and new antibodies, have reported that CAT is localized within large aspiny or small multipolar cells in the striatum.

AChE: Whereas controversy clouds histochemical studies of CAT, AChE remains one cholinergic substance that apparently has been demonstrated reliably and validly with current histochemical procedures (6). Indeed, recent developments in histochemical protocols for the enzyme have permitted improved morphologic detail to be obtained (6). The pharmacohistochemical regimen of Butcher et al. (12), for example, derived essentially from the observations of Nichols and Koelle (34,35) that AChE reappears first in the somata of retinal amacrine cells following irreversible enzyme inhibition by bis(1-methylethyl)phosphorofluoridate, has been used by many different laboratories to "rewrite" the AChE neuroanatomy of the brain (e.g. 19,36,37).

Acetylcholinesterase and Cholinergic Neurons

Beginning with the development by Koelle and Friedenwald (26) of a sensitive histochemical method for AChE, there has been speculation concerning to what extent the presence of the enzyme in neural tissue could be used as a marker for cholinergic neurons (i.e. those containing and utilizing acetylcholine [ACh] as a neurotransmitter; see 10). Although most researchers investigating cholinergic mechanisms realize that the mere presence of AChE within and/or on a particular neuron is not a sufficient condition to label that neuron cholinergic (see 10), hypotheses have been formulated attempting to relate the intensity of AChE staining to the simultaneous presence of ACh and, by implication, its synthetic enzyme, CAT. One such proposal, which for want of a better appellation