Meeting Report: Workshop of the International Study Group (ISG) on the Pharmacology of Memory Disorders Associated with Aging

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An International Study Group (ISG), formed to facilitate research into possible treatments for memory disorders associated with aging and the dementias, held its initial workshop in Zurich, Switzerland, from November 30 to December 2, 1979. It was attended by approximately sixty scientists and research administrators from the United States, Canada, and Western Europe, and its program was arranged by a committee consisting of Richard Wurtman and Suzanne Corkin of M.I.T. and John Growdon of the Tufts–New England Medical Center. One purpose of the workshop was to determine whether a consensus exists concerning the natural history of age-related memory loss, and whether available clinical and neuropathological data allow the classification of patients with memory disorders into groups that might predict their responses to proposed treatments. Another was to discuss the methods currently used in various centers to quantitate memory defects, and to see whether a uniform testing procedure can be established that will facilitate comparing data obtained at different institutions. A third was to discuss the fragmentary evidence concerning the utility of dietary lecithin or cholinergic drugs for treating memory disorders, and to foster a dialogue with lecithin manufacturers leading to the production of lecithins that are sufficiently pure for clinical use.

In December, 1978, an international meeting was held in Tucson, Arizona, to review the evidence that the administration of choline or lecithin to animals could enhance brain acetylcholine synthesis, and
thus might be useful in treating brain disorders in man associated with inadequate cholinergic transmission (for example, tardive dyskinesia, Friedreich's ataxia, mania, and memory loss). The wealth of data available at the time that earlier meeting was planned seemed to warrant publishing the proceedings; this volume ("Choline and Lecithin in Brain Disorders", edited by A. Barbeau, J. H. Growdon, and R. J. Wurtman; Raven Press, New York) appeared late in 1979. In contrast, it was not anticipated that significantly more data would be available at the time of the Zurich meeting than had been summarized in the above book, or in other recent volumes (e.g., Alzheimer's disease: Senile Dementia and Related Disorders, edited by R. Katzman, R. D. Terry, and K. L. Bick; Raven Press, New York); hence no book was planned to follow the ISG workshop. Inasmuch as the topics discussed in Zurich and the preliminary data presented on drug trials are of general interest, a synopsis of the presentations follows.

A central theme underlying the ISG workshop was the hypothesis that some cholinergic neurons—perhaps those in the septohippocampal tract—have a central role in the formation and retention of new memories; that central cholinergic transmission is impaired in certain types of memory disorders (i.e., those associated with aging or with Alzheimer's disease); and that lecithin, choline, or other agents that increase cholinergic tone might thus ameliorate the memory loss associated with these disorders. There is ample precedent for using a neurotransmitter precursor to "replace" missing neurons. For example, L-Dopa (a dopamine precursor that, unlike choline or lecithin, is not normally found in the diet or circulation) reverses the clinical findings of Parkinson's disease, probably by restoring the diminished levels of dopamine in the Parkinsonian striatum. As shown by numerous investigators, Alzheimer's disease is also associated with a perhaps-selective loss of a specific neuronal population—in this case, cholinergic: Brain levels of the enzyme choline acetyltransferase (CAT), a marker for cholinergic neurons, are markedly diminished in patients with this dementia, while postsynaptic cholinergic receptors are unaffected. That acetylcholine release is essential for normal human memory function is suggested by findings that the blockade of central cholinergic receptors (with scopolamine) can markedly worsen memory function in a pattern closely resembling that seen in aging and Alzheimer's disease, whereas the administration of physostigmine, a cholinesterase inhibitor that enhances central cholinergic transmission, can reverse this impairment.

The use of lecithin or choline to treat neurological diseases is a direct outgrowth of the finding that oral administration of these