

even with severe and long-lasting jaundice, do not show any bilirubin deposits in the CNS, except for that of the choroid plexuses and CSF. One of the explanations for this age difference with respect to the deposition of bile pigments is that the newborn brain is physiologically underdeveloped and its blood-brain barrier is more permeable, in contrast to the fully developed and "leakproof" blood-brain barrier of the mature brain.

Systematic studies of the blood-brain barrier mechanisms in the aging brain have not been reported. However, one can assume that such alterations may occur since glial cells proliferate and water decreases with advanced age (29), thus possibly re-

sulting in a decrease in extracellular space. Additionally, changes in the permeability of the cerebral capillaries with aging (29) can contribute to alterations of the blood-brain barrier at this time.

NEUROTRANSMITTER CHANGES WITH AGE

One of the biochemical substrates underlying integrative capacity in the maturing and aging CNS is that responsible for neurotransmission. Regardless of the speed with which information is transmitted from neuron-to-neuron or neuron-to-glia-to-neuron, it is assumed to involve neurotransmitter substances.

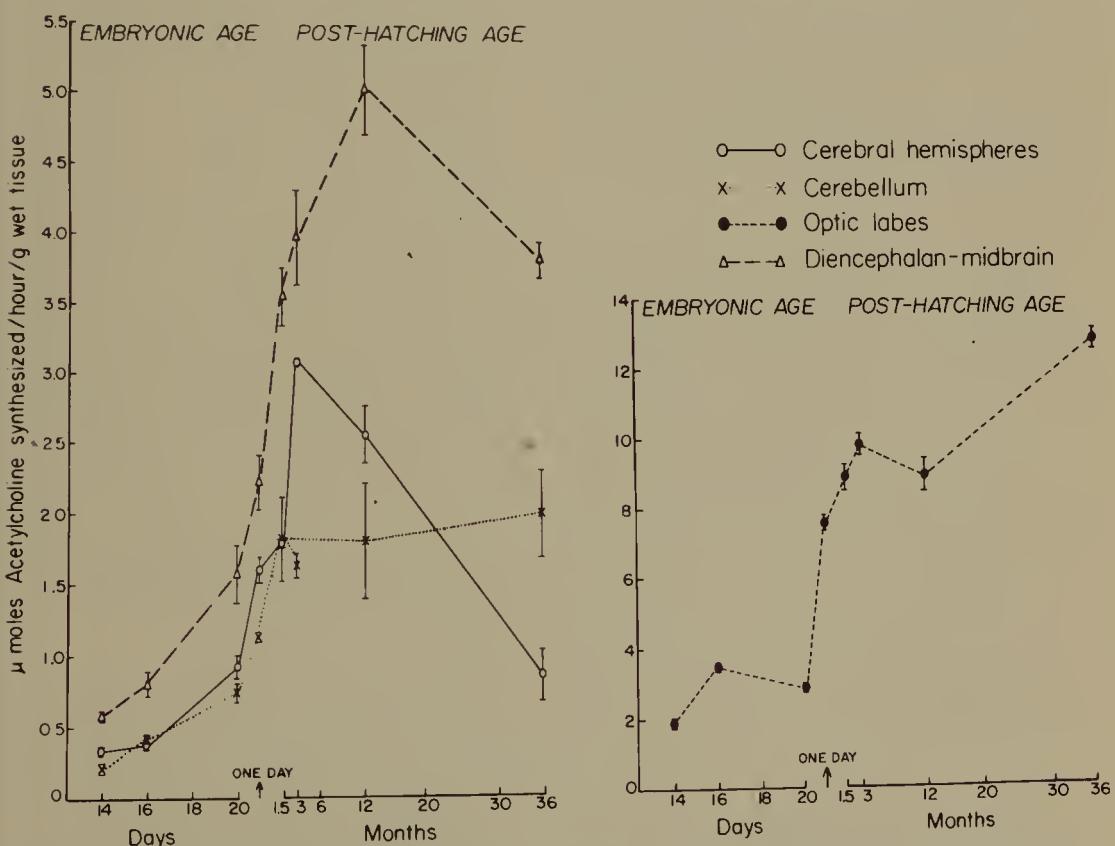


Figure 3. Changes in choline acetyltransferase activity expressed as μ moles of acetylcholine synthesized per hour per gram wet tissue in the four CNS structures of chicks during embryonic age (days) and post-hatching (months). Points as in Fig. 1. (From Vernadakis (33).)

Some aspects of cholinergic, monoaminergic, and amino acid neurotransmission and the changes occurring during development and aging will be discussed.

Cholinergic system

The activities of acetylcholinesterase (AChE) and choline acetyltransferase (ChA), the hydrolyzing and synthesizing enzymes of acetylcholine (ACh), respectively, have been used as indexes of cholinergic neurotransmission. In the chick, the activity of AChE increases markedly in both the cerebral hemispheres and cerebellum from embryonic age up to 3 mo after hatching, and from 20 mo up to 36 mo posthatching (Fig. 2) (33). The activity of ChA increases in the cerebral hemispheres up to 3 mo after hatching (Fig. 3), and then decreases reaching embryonic levels by 3 yr; in the cerebellum ChA increases up to 6 wk posthatching, and then levels off. Studies by

Timiras and associates (29) in the rat have also shown that ChA does not markedly change in the cerebellum and cerebral hemispheres from 2 mo up to 20 mo, whereas it markedly decreases with age in the spinal cord (Table 1). It is now generally accepted that the presence of ChA is a more conclusive index for the presence of ACh. On this basis the low levels of ChA activity in the aging cerebral hemispheres and spinal cord would suggest that cholinergic neurons are at a very low level of activity or have decreased in number.

Acetylcholinesterase has been proposed to have a dual function during maturation. Filogamo and Marchisio (9) speculate that the early ACh system, namely ACh itself, ChA and AChE, may be one of the pathways involved in some way in the complex process of nervous system development through mechanisms that are not yet adapted to synaptic transmission. We further propose from our findings that the sharp rise in AChE activity with aging, particularly in cerebral hemispheres (Fig. 2), may present a function of AChE other than its role in neurotransmission processes. For example, one can visualize the ACh system having a humoral function during aging and thus explain the high levels of AChE. The low levels of ChA in the cerebral hemispheres during aging reflect a decrease in cholinergic neurons, a finding which supports the idea of a humoral role for AChE at this life stage.

Since glial cells markedly proliferate during aging, another possibility that could explain the high levels of AChE is that glial cells may also contain AChE. Although Giacobini (10) has reported that glial cells do not contain specific ChE (AChE), the possibility that some AChE may be present in glial cells has not been

TABLE 1. Changes in choline acetyltransferase activity in CNS areas of the rat with age^a

Age, months	μ Moles of [¹⁴ C]acetylcholine synthesized/hour per g wet tissue		
	Cerebellum	Cerebral cortex	Spinal cord
2	0.56 ± 0.05 ^b (16)	3.57 ± 0.23 (11)	6.39 ± 0.24 (13)
12	0.62 ± 0.04 (16)	3.65 ± 0.06 (16)	5.85 ± 0.30 (16) <i>P</i> < 0.01 ^c
20	0.59 ± 0.03 (11)	3.29 ± 0.13 (11)	5.00 ± 0.26 (11) <i>P</i> < 0.001 ^c <i>P</i> < 0.05 ^d

^a From Timiras (29). ^b Values are means ± SE (number of determinations shown in parentheses; one determination per animal.) ^c Significance of difference from 2-months-old. ^d Significance of difference from 12- to 14-months-old.