Gorini's group and others have evidence which indicates that each structural gene has its own operator site—in other words they are not in one operon. All the operators bind the same repressor protein—a product of the single repressor gene—but apparently with differing affinities, because although control of all the structural genes is parallel it is not coordinated, and the structural genes are derepressed to different extents by temperature sensitive repressors. If all the operators had the same affinity for the repressor, they would, of course, give identical responses to a temperature sensitive repressor.

As Jacoby and Gorini point out, the independent control of the eight structural genes allows a greater degree of flexibility in regulating the amount of each individual enzyme than would be possible if the genes were all in one operon. The arginine pathway is in effect a multi-operon system.

In the second paper, Karlstrom and Gorini (*ibid.*, 89) marshal physiological evidence in support of this scheme. In strain B, synthesis of ornithine transcarbamylase, one of the enzymes of the pathway, is increased in the presence of excess arginine, but only if the bacteria are grown at temperatures below 39° C. Above this temperature, arginine actually represses enzyme formation, whereas temperature has no effect on regulation of enzyme synthesis in strain K. This and other physiological evidence suggests that physiological conditions affect the state of the strain B repressor and alter its affinity for the operator sites. Thus the physiological evidence supports the genetic evidence that in *E. coli*, B and K control of the arginine pathway is basically the same. The end-product, arginine, by activating a repressor protein, causes repression of arginine biosynthetic enzymes, a case of end-product repression.

NEUROCHEMISTRY

Brains New and Old

from a Correspondent

THERE are considerable problems involved in studying the ageing human brain, and some of these were made apparent at a symposium organized by the British Society for Research on Ageing on January 23 at the Wellcome Foundation, London. These difficulties contrast with the progress reported by scientists working on the biochemistry of the developing brain. Morphological changes in the senile brain are, with only one known exception, restricted to man, whereas observations of the developing brain of experimental animals give a valuable insight into the development of the central nervous system of man.

Changes in the composition and metabolism of lipids in the developing brain can now be described in considerable detail (G. B. Ansell). The brain is unusually rich in lipids, almost all of which are present in membranes, especially those comprising the myelin sheath. The synthesis of cerebroside, phosphatidal ethanolamine and triphosphoinositide coincides with myelination, and changes in the concentration of these lipids serve as a sensitive index of alterations in the formation of the myelin sheath. Thus, during the vulnerable period of brain development, retardation of myelination by hypothyroidism (R. Balázs) or by mild undernutrition (J. Dobbing) can be readily assessed by analysing the lipids of the whole brain. In hypothyroidism, reduced myelin formation is accompanied by reductions in succinic dehydrogenase activity. This suggests an additional effect on nerve ending particles. Balázs and his colleagues also found that lack of thyroxine retards the age related process of synthesis of dicarboxylic amino-acid from glucose. Dobbing found that although starvation of adult animals produced no detectable change in the mature brain, even mild undernutrition for three weeks resulted in permanent changes in the concentration of cholesterol in the brains of newborn rats. The possible relation between such restricted brain growth and subsequent intellectual development is intriguing, and here there may eventually be some common ground between those studying the effects of malnutrition and hypothyroidism in the developing brain and intellectual deterioration in the elderly.

Although early labelling experiments supported the concept of the inertness of neuronal DNA, it now seems that metabolically active DNA is also present in the nucleus (S. R. Pelc). ^{3}H-Thymidine can be incorporated into DNA even when premitotic nucleic acid synthesis is known not to occur. Although the nerve cell does not divide, the neurone with its dendrites has an enormous surface membrane area which is susceptible to continual wear and tear. It is tempting to suggest (K. C. Dixon) that breakdown of the lipoprotein of the plasma membrane can be related to the accumulation within the ageing neurone of the lipoprotein pigment lipofuchsin. It has been suggested that lipofuchsin may be produced by peroxidation of lipid and that its appearance may be related to a deficiency in vitamin E. Presumably the accumulation of lipofuchsin within the nerve cell body leads to an impairment of neuronal metabolism which contributes to the ageing process.

Brain atrophy with grossly enlarged ventricles is found in some cases of dementia (J. A. N. Corsellis). Although senility in the aged is sometimes related to atherosclerosis of the large vessels, more than half the cortex may be destroyed before mental impairment becomes apparent. Qualitative examination of the senile brain suggests that there are not only fewer neurones than in the normal brain, but also that characteristic degenerative changes occur. Argyrophilic plaques, also seen in pre-senility (Alzheimer's disease), are present, as well as neurofibrillar tangles. In demented patients there are usually more plaques and tangles than in normal controls (A. T. Dayan). M. Roth emphasized the importance of quantifying these neuropathological changes in relation to mental behaviour. Such correlations demand standardized methods for the measurement of intellect in the aged (R. D. Savage) applied to rigorous quantitative histology. Using such methods, highly significant differences in plaque count were obtained in the brain of subjects with dementia compared, but with other diseases of the brain no such differences were seen.

It seems a pity that this important work on human senility is not supported by the kind of intensive interest shown by British neurochemists in the developing brain. The problem is simply that the experimentalist has no suitable model for investigations on senile dementia. We must therefore wait until the time when such changes can perhaps be induced artificially in the brains of laboratory animals.