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The pathology of dementia

A study of the diverse aspects of the pathological process begins logically with the changes that are undergone by the ageing normal brain. The discussion in this section is based on accounts provided by Armbrustmacher (1979), Tomlinson (1979), Bowen and Davison (1981), and Shaw and Meyer (1982).

The human brain increases four-fold in weight during the first 3 years of life, then steadily to about the age of 18. The first significant signs of decreasing weight are seen about 45 years and the decline continues into the eighties. It is believed that neuronal degeneration and replacement gliosis result in an average reduction in brain weight of 11% over five decades.

Apart from the decrease in brain weight and volume, the most obvious naked-eye change with advancing age is the increasing prominence of gyral atrophy. The greatest loss of weight occurs after the age of 60 in normals but the contribution of various degenerative processes to the picture has to be allowed for to an increasing extent after that age. It has also to be kept in mind that there has been a secular change in human size, analogous to that for cognitive processes, over several generations. Mean human heights have increased over the past 50 years as almost certainly has, as Tomlinson (1979) puts it, mean brain weight. Some loss of brain weight in elderly subjects may therefore simply reflect initially smaller brain weight.

In over 50% of normal old brains variable gyral narrowing with sulcal widening is visible, particularly in the parasagittal frontal and parietal, and lateral frontal and lateral temporal cortex; the occipital cortex and all inferior gyri are much less obviously affected.

Hemisphere volume progressively diminishes from the age of 20 years with a greater fall in men than in women. The loss of brain weight is also greater in males than in females. Further, between 20 and 50 years, grey
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matter volume falls more than white, but after that more white matter is lost than grey, which workers tend to equate with neuronal loss.

Evidence now exists that cortical neurones, cerebellar Purkinje cells and spinal cord motor neurones are all diminished in normal old age but that various brain stem nuclei have their nerve cells virtually intact throughout life.

As well known, cells of the central nervous system are at their maximum number at birth. There is then a progressive age-related decrease in cell population which begins about the age of 20–25, the end of the period of growth and maturation.

Some areas of the cortex are affected to a greater degree than others. Neuronal loss is particularly significant in the superior frontal gyrus, the superior temporal gyrus, the full extent of the precentral gyrus and the visual cortex. In frontal and temporal areas this neuronal decrease is approximately 40% by the ninth decade, which, it is thought, might account for the benign forgetfulness, slower motor performance and other physiological changes among the normal elderly.

Although neuronal loss occurs in all cortical layers, they are most marked in layers 2 and 4. These two layers of the cortex are the last to appear during development, indicating a possibility that a link might exist between the sequence of appearance of structures in the central nervous system and their ability to withstand the rigours of the normal ageing process.

As we have seen, the brain stem structures are not involved in the process of age-related neuronal loss, with the exception of the locus coeruleus. The rate of neuronal loss in the nucleus of this structure is said to parallel the rate of cell loss in the cortex. Since this structure is believed to be involved in the regulation of sleep, this finding is of particular interest with respect to the abnormal sleep patterns including insomnia found among the elderly who generally experience a reduction in the duration of sleep, decreased REM (dream) sleep, dreaming and stage 4 (deep) slow wave sleep.

At a more basic level, loss of brain substance is reflected by a decrease in myelin, RNA, sodium and potassium while calcium and iron increase; O₂ consumption, too, decreases with age. As was shown in Chapter 6, xenon-133 inhalation cerebral blood flow studies have shown a gradual reduction in hemispheric weight of grey matter with advancing age in normal healthy adults. The lateral ventricles tend to become enlarged, the cortical gyri narrowed and the sulci enlarged. Ventricular measurements based on CT scanning (see Chapter 4) have revealed a gradual increase in ventricular size, with the greatest increase occurring in the eighth and ninth decades.

Microscopy of cerebral blood vessels suggests there are alterations in the cerebral microvasculature in the form of ‘corkscrewing’, ‘spiralling’ and ‘coiling’ of the perforating cortical arteries, arterioles, capillaries and venules. These alterations seem to occur throughout the cerebral cortex and subcortical matter and become more obvious with each passing decade of life. Naked-eye and microscopic observations also reveal increased opacification and loss of tubular resiliency of the vessel walls of all sizes with age.