Morphometric Comparison of Hippocampal Microvasculature in Ageing and Demented People: Diameters and Densities

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Summary. The diameters and densities of capillaries and arterioles in the hippocampal cortex of normal subjects and patients with Alzheimer’s dementia were measured in thick celloidin sections stained for alkaline phosphatase. Microvascular diameters in general are affected more by age than by the presence of dementia of the Alzheimer type. The diameter of both capillaries and arterioles increases significantly with age. The density of capillaries decreases whereas that of the arterioles increases significantly. The capillary changes suggest that a reduced exchange potential accompanies ageing.

In brains of people with Alzheimer’s disease the overall capillary diameters and densities do not differ from those of age-matched controls. Regional changes may, however, be important: those hippocampal zones showing the greatest severity of or increment in nerve cell lesions do correspond to those having the highest levels of or increase in capillary density and the greatest decrease in diameter, suggesting a direct association between neuronal susceptibility to Alzheimer changes and degree of regional blood supply. Capillary surface areas, volumes, and area/capillary volume ratios support the possibility of this relationship.

Neurofibrillary tangles and granulovacuolar degeneration do not correlate equally with the degree of capillary “irrigation”: tangles are more closely related to these morphological vascular parameters.

Key words: Dementia — Hippocampus — Alzheimer’s disease — Ageing — Microvasculature

Introduction

Changes in the microvascular anatomy of the human brain have occasionally been observed in association with the ageing process. Hassler (1967) described “glomerular loops”, “bundles”, and “wickerworks” (after Cerletti 1910/1911). Fang (1976) also saw coiling and looping of the small vessels, with knob-like formations and sinusoidal enlargements of the venules, as well as areas of apparent decreased vascularity. Ravens (1978) confirmed earlier observations of tortuous changes in ageing small vessels. Beskow et al. (1971) found that vascular “loops”, “bundles”, and “wickerworks” do not occur in greater numbers in patients with senile dementia than in the normal aged population. A few non-specific pathologic changes in small cerebral vessels that are associated with ageing and dementing illnesses have also been mentioned by McMenemy (1971), Jellinger (1977), and O’Brien (1977).

Despite such descriptive reports, very little information is available about quantitative changes in the cerebral microvasculature either attributable to ageing, or associated with the pathology of senile dementia of the Alzheimer type. In the human neocortex Hunziker et al. (1979), using an image analyzer, found that capillary diameter, density, and volume increased in the 65—74-year-old group, while surface area decreased; values for still older subjects resembled the young. Bär (1978, 1980) reported that ageing in the rat produced little change in capillary diameters, an increase in their density and surface area, and a decrease in their volume.

The neurofibrillary tangle of Alzheimer (1907), granulovacuolar degeneration of Simchowicz (1910/1911), and neuronal fall-out all occur in the normal aged person’s hippocampus, but are many times more severe when the memory disturbance of senile dementia of the Alzheimer type (SDAT) is super-imposed. The severity of such changes in the human hippocampus in ageing and Alzheimer’s disease has been quantified in our laboratory (Ball 1976, 1977; Ball and Lo 1977).

Regional variations in the hippocampal density of tangles and granulovacuoles, and also of the rod-like
Fig. 1. Micro-anatomy of the hippocampal formation, showing the six cortical zones surveyed: entorhinal area; presubiculum; subiculum with medial H1 (or prosubiculum); lateral portion of H1; H2; endplate (H3, H4, and H5)

bodies of Hirano (Hirano et al. 1968), have also been noted (Ball 1978a, b). The microscopic anatomy of the human hippocampal pyramidal cortex can be divided into six “zones” (Fig. 1): the entorhinal area (including the parasubiculum and the parahippocampal gyrus); the presubiculum; the subiculum together with the medial portion of Rose’s H1 field (prosubiculum); the lateral portion of H1 (the Sommer sector, which corresponds to Lorente de Nó’s CA1); H2; and the endplate (H3, H4, and H5). The relative topographic severity of the neuronal lesions of neurofibrillary tangles and granulovacuolar degeneration, as well as of the rod-like bodies of Hirano can thus be assigned a (representative) rank order for ageing and dementia (Ball 1978a, b). Comparison of these rank orders has shown that of the six zones, those three most severely affected by neurofibrillary tangles and granulovacuolar degeneration, as well as of the rod-like bodies of Hirano can thus be assigned a (representative) rank order for ageing and dementia (Ball 1978a, b). Comparison of these rank orders has shown that of the six zones, those three most severely affected by neurofibrillary tangles and granulovacuoles, the order is: subiculum > H1 > H2. For Hirano bodies, the order is: H1 > subiculum > H2. The increased predilection of the H1 zone and adjacent subicular area in both ageing and dementia is notable, and has confirmed earlier observations of such regional predispositions by Hirano and Zimmerman (1962), Woodard (1962), Jamada and Mehrain (1968), Corsellis (1970), Tomlinson and Kitchener (1972) and Hooper and Vogel (1976). This remarkable pattern of regional hippocampal susceptibility resembles the “selective vulnerability” of neurons in the H1, subiculum and endplate in hypoxia, ischemia and epilepsy, as first described by Spielmeyer (1925) and Uchimura (1928a) and recently reiterated by Brierly (1976) and Corsellis (1976). Vogt and Vogt (1937) ascribed this phenomenon to regional variations in parenchymal “physico-chemical” characteristics, but Uchimura (1928b) suspected some regional arrangement of arterioles. Neither the vascular nor the “pathoclisis” hypothesis has been proven or refuted effectively (Altschul 1938; De Reuck et al. 1979).

Previous studies of the hippocampal vascular bed have either described patterns of distribution in the human (Uchimura 1928b; Hens and Van den Bergh 1977), in the rabbit and monkey (Lorente de Nó 1927) and in the rat (Coyle 1978), or have reported capillary measurements for a given age group in the rabbit (Cobb 1929), in the cat (Craigie 1930), in the child and dog (Mao Tseng-jung 1959). To explore the possibility of some correlation between the regional vasculature and the distribution of neuronal lesions in the hippocampi of aged and demented subjects, we have examined the anatomy of the blood vessels of the hippocampi in human post-mortem material. The study includes analyses of: (a) the angioarchitecture of the major arterial branches of the circle of Willis supplying the hippocampal formation; (b) the diameters of the microvasculature within the