
There is confusion in the literature on the frequency of sclerosis within Ammon’s horn in people with epilepsy. Evidence that this same neuropathological appearance is seen in cases of psychosis complicating senility or cerebrovascular disease, and in general paralysis of the insane and cases of mental deficiency, further undermines confidence in the interpretation that Ammon’s horn sclerosis has anything specific to do with epilepsy. Using resources available to him as pathologist to mental hospitals in southern England, and gathering together material from Runwell Hospital, St Faith’s Hospital and Harold Wood Hospital (all in Essex, UK), Dr John Arthur Nicholas (Nick) Corsellis (1915–94) aims to describe the frequency of hippocampal sclerosis in a somewhat selected autopsy sample, and thereby to reconcile issues relating to its role in epilepsy.

Of 200 cases studied, all but 28 autopsies are from individuals who were confined to mental hospitals in life. Their diagnoses were as follows: non-organic psychoses, \( n = 65 \); mental deficiency, \( n = 14 \); cerebrovascular disease and psychosis, \( n = 30 \); Alzheimer’s disease, \( n = 29 \); other brain diseases, \( n = 30 \); and epilepsy, \( n = 32 \). Sixty-four of the 200 individuals are known to have had at least one convulsion at some stage during their life. First, Dr Corsellis considers the frequency of any abnormality in Ammon’s horn in groups defined by clinical category (Fig. 1). Five of 65 people having ‘no known organic basis’ (normal or neurotic individuals, \( n = 19 \); schizophrenia and paranoia, \( n = 33 \); affective psychosis, \( n = 13 \)) have ischaemic lesions. Three others from this group with a history of convulsions in life have normal neuropathological findings. Fourteen cases are considered to have been mentally defective (tuberose sclerosis, \( n = 2 \); gargoylism, \( n = 2 \); mongolism, \( n = 2 \) and other disorders, \( n = 8 \)). Lesions of Ammon’s horn include one example each of local atrophy, sclerosis and necrosis. Four other cases with mental deficiency but no neuropathological abnormality had convulsions in life. In the group with systemic or localized cerebral arteriosclerosis, 13 of 30 have gross vascular lesions in Ammon’s horn. Of these, most \( (n = 11) \) were hypertensive in life compared with 9 of 17 without an abnormality of Ammon’s horn. In the Alzheimer’s disease and senile psychosis category, 16 of 29 have a local lesion (unspecified) in Ammon’s horn. Of the 30 with miscellaneous organic cerebral conditions (tumour, \( n = 8 \); syphilis, \( n = 4 \); Huntington’s disease, \( n = 3 \); Pick’s disease, \( n = 2 \); Jakob-Creutzfeld disease, \( n = 2 \); others, \( n = 11 \)), of whom 11 had epilepsy in life, abnormalities of Ammon’s horn are found in three: these include reactive changes to a local ependyma, focal infarction, and neuronal loss with gliosis. Lesions of Ammon’s horn are found in 15 of 32 individuals with cryptogenic or symptomatic epilepsy as the primary clinical disorder.

How should these descriptive observations be interpreted? The frequency of lesions in Ammon’s horn ranges across the six groups from 8% in the normal or neurotic cases to 55% in senile psychosis and Alzheimer’s disease. Convulsions have occurred during their lifetime in 26 of 55 (47%) individuals with a lesion in Ammon’s horn. Yet lesions of Ammon’s horn are no more frequent in the group with epilepsy than in patients with arteriosclerosis or dementia. Does this lack of discrimination support the view of Morel and Wildi (Acta Neurologica Belgica 1956: 56; 61–74) reporting broadly similar results that ‘the importance of damage to Ammon’s horn in epilepsy has been greatly exaggerated…in fact it appears that no relation exists between Ammon’s horn sclerosis and epilepsy’? But these sweeping statements depend on how cases and lesions are categorized, a matter on which Dr Corsellis has views: ‘A diagnosis of epilepsy is not the same thing as the occurrence of one or more convulsions…The term Ammon’s horn sclerosis has been taken to include any pathological lesion of this area…the problem is not necessarily the demonstration of a link between a convulsion and any lesion of the horn’. It is better to consider separately those individuals with cryptogenic epilepsy and a history of recurrent seizures. Therefore, a more detailed analysis of the material is now provided (Fig. 2).

First, different grades of damage to Ammon’s horn must be considered: ischaemic nerve cell change with neuronal loss and astrocyte proliferation; the same but with intense gliosis and shrinkage (classical Ammon’s horn sclerosis); areas of focal infarction with diffuse vascular change; and localized neuronal atrophy, without loss of volume, and neurofibrillary tangles and senile plaques in surviving nerve cells. Reclassification of cases in the acute ischaemic category includes five (of the original 65) examples of normal or neurotic syndromes; one each from those with mental deficiency \( (n = 14) \) and arteriosclerosis \( (n = 30) \); and three from the group with epilepsy \( (n = 32) \). Corsellis cannot improve on the interpretation of Lindenberg (J Neuropathology 1955: 14; 223–243) that there is an unbreakable circle of ‘structural brain lesion’, ‘anoxia’ and ‘convulsion’ in which any one element may
precipitate the others: ‘the fact remains that acute lesions of Ammon’s horn may be found both as a sequel to anoxia and as an accompaniment of convulsions . . . if the patient survives long enough, the end result will be a scar, that is a sclerosis’. Fifteen cases (four with bilateral lesions) have Ammon’s horn sclerosis; of these, 13 were originally classified in the epilepsy group (three with bilateral lesions) and one each to the category of mental deficiency (with both sides affected) and senile dementia. Thus, a total of 19 Ammon’s horns in 15 patients show sclerosis. The combined pathological categories of focal infarction and plaque and tangle formation, sometimes occurring in association, encompass all the examples of cerebral arteriosclerosis (typically showing unilateral hippocampal lesions) and senile psychosis (usually bilateral). Older patients are over-represented in these two groups and the onset of epilepsy has occurred late in their clinical course. Conversely, the group with cryptogenic epilepsy is younger and the convulsions are likely to have been lifelong (average duration 34 years). Even though several patients had experienced convulsions shortly before death, no one shows acute ischaemic changes in Ammon’s horn. As to timing of the insult, the debate is not settled on whether anoxic damage is strictly birth related or the result of post-natal events. All that can be said is that ‘Ammon’s horn sclerosis [is] correlated with a history of convulsions occurring in infancy or in early childhood’. Therefore,

Figure 1  (A) Normal Ammon’s horn with the fields h1 to 5 indicated. (B) Ammon’s horn with pale, swollen h1 field and apparent disappearance of nerve cells. The nerve cells are in fact still present but are shrunken and many have stained faintly. (C) Classical Ammon’s horn sclerosis from cases of cryptogenic epilepsy, showing the almost complete loss of nerve cells, apart from h2 and the dentate gyrus, and an even distribution of glial nuclei throughout the affected area. (D) A small circumscribed scar in h1/h2, the result of an infarct due to arteriosclerosis. (E) The pale, moth-eaten appearance of the h1 field, with decimation of the nerve cell population in a case of senile dementia (A–E: cresyl violet, ×11).
Dr Corsellis finally examines his material, without statistical analysis, for any association between Ammon’s horn sclerosis and age at onset of convulsions: a strong correlation is seen, among 27 cases in which sufficient information is available, between symptomatic or cryptogenic epilepsy in childhood and the presence of Ammon’s horn sclerosis. On the severity of the epilepsy-related anoxic insult, nothing much can be said.

Dr (later Professor) Nick Corsellis takes the view that ‘it is not easy to examine the post-mortem material of a mental hospital and yet look on the association of epilepsy and changes in the Ammon’s horns as either infrequent or irrelevant’. He shows that sclerosis in this part of the hippocampus may occur in various clinical contexts but is especially associated with lifelong cryptogenic epilepsy. As papers in the current issue make clear (page 3764 and 3778), the consequences for electrical activity throughout the cortex, the clinical expression of such discharges, and the molecular consequences of seizure activity for the structure of Ammon’s horn remain matters of research interest in contemporary neuroscience.

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Figure 2 (A) ‘Ischaemic change’ affecting most of the nerve cells of the h1 field. (B) Part of h1 field of the Ammon’s horn showing necrotic remnants of nerve cells and marked microglial proliferation. (C) Coronal cut through a temporal lobe from a case of cryptogenic epilepsy showing a sclerosis of Ammon’s horn with adjacent areas, both of older damage and of recent haemorrhage (×1.3). (D) Neurofibrillary tangles and formation of senile plaques at subicular end of h1 field (A and B: cresyl violet, ×230; D, ×210).