Neuropathology of epilepsy and psychosis: the contributions of J.A.N. Corsellis

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Professor J.A.N. Corsellis, whose life and work is recalled here, gained great insight into the meaning of morphological cerebral aberrations found in neuropsychiatric disease through exact neuropathological investigations of tissue specimens obtained from patients with distinct syndromes. He was a leading authority in the field. We have searched and compiled resources relating to J.A.N. Corsellis’ life and work, including personal memories from colleagues and data from scientific publications. J.A.N. Corsellis made seminal contributions to the understanding of neuropsychiatric disease; his works substantially added to the understanding of the dementias, schizophrenia and the psychoses, and morphological sequelae of boxing. In seizure disorders, his name is linked to the first description of focal cortical dysplasia and limbic encephalitis, the pathology of status epilepticus and Ammon’s horn sclerosis, and the systematic investigation of epilepsy surgery specimens in general. Both his life and work are closely linked to Runwell Hospital, Wickford, Essex and the Maudsley Hospital. During his professional life he established a large brain bank, now known as the Corsellis Collection. J.A.N. Corsellis had significant impact on neuroscience; many of his observations were groundbreaking and are still valid.

Keywords: epilepsy; psychosis; neuropathology; Corsellis

Abbreviation: ECT = electroconvulsive therapy

Introduction

Our knowledge concerning major neurological diseases has grown, supported by precise clinicopathological correlations by diligent pathologists through their work on autopsy material and surgical specimens. The fundamental changes concerning the aetiology and pathophysiology of disorders, once classified as ‘functional’, were driven by neuropathological insights. Eminent contributions to the understanding of the underlying processes in these fields were made by John Arthur Nicholas Corsellis (1915–1994),
who worked at Runwell Hospital, Wickford, Essex and the Maudsley Hospital in London. His name is linked to the recognition of focal cortical dysplasia as an entity of seizure aetiology (Taylor et al., 1971), the first description of limbic encephalitis (Brierley et al., 1960), systematic studies on Ammon’s horn sclerosis (Corsellis, 1957; Margerison and Corsellis, 1966), temporal lobe epilepsy and epilepsy surgery in general (Falconer et al., 1964; Corsellis, 1970) and first systematic studies on the pathology of status epilepticus (Corsellis and Bruton, 1983). His work on epilepsy was in close collaboration with Murray Falconer at the Maudsley Hospital. Concerning the pathology of psychosis, his work pioneered systematic morphological research in psychiatry (Corsellis, 1972) especially schizophrenia (Brown, 1986) and the dementias (Corsellis, 1962, 1975, 1976, 1977, 1979, 1986). Furthermore, his studies clarified the cerebral consequences that caused the dementia of some professional boxers (Corsellis et al., 1973). Here, we commemorate this great man and his contributions to the neuropathology of epilepsy and the psychoses, along with aspects of his personal life and the historical context. The material presented here is compiled from diverse resources such as scientific manuscripts, journal publications including society announcements, book chapters, book reviews, obituaries and, as a main source, the personal memories of friends and colleagues.

J.A.N. Corsellis (1915–1994)


John Arthur Nicholas Corsellis (Fig. 1), often called Nick, ‘started his career by reading modern languages at Cambridge, and lived for a time in pre-war Germany. His deep compassion was stirred by events around him, drawing him towards the human and social sciences. Back in London, in his early twenties, he took up the study of medicine at the London Hospital’ (Birley, 1989). He qualified from London Hospital in 1944 (Janota, 1995).

But soon disaster struck. He fell victim to tuberculosis in the pre-streptomycin era while working on the wards, and much of his time for the next decade was spent in sanatoria and hospitals. The imposed bed rest laid the foundations for an astonishing career. He read neuroanatomy while immobile and learned pathology in the laboratories of the sanatoria during periods of convalescence. Rarely can prolonged illness have had such magnificent pay-off. Not until his mid-30s was he able to take up permanent employment. (Birley, 1989)

Being forced to apply for a theoretical medical discipline as a result of his tuberculosis infection excluded him from patient contact. His early career took place in psychiatric service at Runwell Hospital. It was there that he came into contact with a group of researchers of all disciplines that had been assembled by the physician superintendent Rolf Strom-Olsen (T.J. Crow, personal memory). Rolf Strom-Olsen (1902–1986) had been the first physician superintendent at Runwell, incorporating the basic sciences like physiology, pathology, neuropathology and biochemistry into the hospital’s activities (Unknown, 1986).

It was Strom-Olsen’s suggestion that Corsellis should consider moving in the direction of pathology. This he was by temperament well able to do. He can be seen as part of a tradition, almost extinct in the middle decades of the century, of an interaction between clinical psychiatry and histopathology and neuroanatomy. The origins of this cross-fertilization were clearly in Germany at the end of the last and the beginning of this century and included such distinguished proponents as Wernicke, von Gudden, Meynert, Alzheimer, Westphal, Nissl, von Monakow and at a later date Kleist and Leonhard. (T.J. Crow, personal communication)

Corsellis himself had spent time in Germany, in particular Munich, at the famous ‘Forschungsanstalt’ under the mentorship of W. Scholz (D. Janz, personal memory). When the impact of these basic sciences again began to be felt in the scientific thought in the second half of the century, Nick Corsellis was a worthy member of this tradition (T.J. Crow, personal memory).

He became registrar and later senior registrar at Runwell Hospital. From 1960 to 1963 he was senior lecturer at the Institute of Psychiatry, when he became consultant neuropathologist at Runwell Hospital (Birley, 1989; see BMJ, 1976). The leaders of the profession soon spotted him. Alfred Meyer gave him access to the Maudsley laboratories and the Institute of Psychiatry. Peter Daniel, succeeding Meyer, consolidated the link’.

He was elected Fellow of the Royal Colleges of Physicians and of Pathologists. He became President of the British Neuropathological Society from 1969 to 1971, and elected president and Professor Hume Adams secretary-general of the International Society of Neuropathology (Birley, 1989; see BMJ, 1978). Not surprisingly in 1976 he was sought out for the Chair of Neuropathology, succeeding Professor P.M. Daniel at the Institute of Psychiatry (Janota, 1995; see BMJ, 1976), which he held with great distinction until his retirement. He took on the mammoth task of sharing in the editorship (of the 3rd and

Figure 1 Professor J. A. N. Corsellis (courtesy of Dr Daniel Lewis-Hodgson, Mindlab® International).
I should describe what he was like: as an individual Nick Corsellis was a critical scientist with a wry and self-deprecating sense of humour and an astute, but basically tolerant, ability to comment on the frailties of human nature. He was a tall, well-built man, with a crumpled face and a subtle and civilized sense of humour. It suited him to be somewhat isolated I think because it gave him a distant view of the rest of the world and humanity. I found him very agreeable. He was certainly very thorough and conscientious in his work and I think was widely regarded within neuropathology by his colleagues. (Crow, 1996, personal memory)

Work on the pathology of epilepsy

Close collaboration with Murray Falconer

During the 1950s, a comprehensive epilepsy surgery programme was developed in London and driven by the activities of Murray Falconer (1910–1977), who in 1949 was announced as the new Director of Neurosurgery at the Maudsley Hospital (Bladin, 2004).

Murray Falconer had a particular interest in brain pathology and the backing of the neuropathology service of the Institute of Psychiatry, a laboratory that can be traced back to the impetus of Victor Horsley (Taylor, 1986). Falconer also had the dexterity to produce an en bloc specimen that rewarded detailed analysis. Most of his specimens from 1951 onwards showed interesting changes that were seen and recorded in detail by a sequence of excellent neuropathologists. (D.C. Taylor, personal memory)

These researchers involved in the programme included Alfred Meyer, John Cavanagh and later J.A.N. Corsellis and Clive Bruton. Furthermore, there was an excellent team of epileptologists at the Maudsley Hospital, including Dr Desmond Pond, Professor Denis Hill and his team, and EEG specialists Maurice Driver and George Dawson (Bladin, 2004; J. Engel, Jr, personal communication). Step-by-step, Corsellis contributed studies focusing on important aspects of epileptology, tissue changes after electroconvulsive therapy (Corsellis and Meyer, 1954; Corsellis, 1957), Ammon’s horn sclerosis (Margerison and Corsellis, 1966) and limbic encephalitis (Brierley et al., 1960; Corsellis et al., 1968; Hierons et al., 1978). In 1964 and 1970, he published excellent reviews on the neuropathology of temporal lobe epilepsy (Falconer et al., 1964; Corsellis, 1970), and in 1971, published the now classic paper on focal cortical dysplasia, with Taylor (Taylor et al., 1971). His close friendship with Murray Falconer is illustrated by a personal letter found in the files at the Corsellis Collection (Fig. 2).

Seminal papers on epilepsy

Cerebral sequellea of electroconvulsive treatment

Among his early works, there is a study in cooperation with Alfred Meyer, his mentor at the Maudsley Hospital (Corsellis, 1991), that they conducted on morphological changes in the context of electroconvulsive therapy (ECT). At that time, ECT was a rather crude procedure and possible irreversible cerebral damage was a matter of ongoing debate (Corsellis and Meyer, 1954). However, data were derived mostly from experimental animal work. Corsellis and Meyer investigated two unique human cases of ECT-treated psychiatric patients deceased by non-neurological cause:

The absence of necrosis in the grey matter particularly in the cornu ammonis and cerebellar cortex indicates... the mild degree of the lesions [found after repetitive ECT]... Such slender histological findings should not, of themselves, be allowed to discredit this form of treatment nor do they provide evidence that this treatment could be the cause of atrophy of the brain. (Corsellis and Meyer, 1954)

This study revealed important evidence that ECT was not necessarily severely damaging to the brain.

Limbic encephalitis

The study by Brierley, Corsellis, Hieron and Nevin (1960) seems to be the first report of an inflammatory reaction within the cerebral hemispheres occurring in association with a carcinoma. The article clearly outlined what today is known as limbic encephalitis:

Involvement of these regions ['the limbic lobes'] were the salient topographical feature in each case, both from the macroscopic and the histological points of view. . . . The histological
appearances were those of a subacute encephalitis without haemorrhage or necrosis. Too little is known, however, either about the aetiology of these newer encephalitides or about the meaning of their peculiar cerebral topography to justify any further discussion of their nosological position. (Brierley, 1960; Corsellis, 1968)

In 1968 Corsellis, Goldberg and Norton reviewed that ‘the aetiology of the encephalitis occurring in association with carcinoma remains obscure, viral, metabolic and immune factors all being easier to invoke than to verify’, and wisely concluded that ‘nevertheless, if a patient suffering from carcinoma, and particularly from bronchial carcinoma, shows evidence of an organic disorder of the mind or even only of the memory, the possibility of an associated “limbic encephalitis” should be considered, whether or not there are other signs of neurological disease’. These two publications, and a subsequent one by Hierons et al. (1978), describe and illustrate the clinical pathology of limbic encephalitis, without too much speculation, and give reference to many interesting resources from before 1960.

Ammon’s horn sclerosis and temporal lobe epilepsy

For decades, the role of the mesial temporal lobes in epilepsy, and morphological changes within Ammon’s horn in particular, were the focus of academic debates regarding the cause of epilepsy (Thom, 2009). A classic controversy (originating with Gower’s refusal to accept Meynet’s description) relates to the interpretation of Ammon’s horn sclerosis as cause or consequence of seizures (Meldrum, 1997). Corsellis’ merit in this context is his strategy to base hypotheses on systematic tissue studies. In his 1957 paper entitled ‘The incidence of Ammon’s horn sclerosis’ Corsellis presented his results from 200 autopsies of different disease groups, including psychoses, dementia and epilepsy (Corsellis, 1957). As one of the main conclusions, he pointed out that ‘... it seems clear that the term Ammon’s horn sclerosis has been used to cover too wide a field, for there is good reason to believe that a number of different morphological entities have been subsumed under this one title’. He emphasized that the precise analysis of the lesion pattern, as shown by his data, allowed for quite precise discrimination of the clinical entities:

... the incidence of [Ammon’s horn] lesions in the group of epileptic patients was roughly the same as that in the senile and the arteriosclerotic groups, but differences both in the morphological appearances of the lesions and in the mechanism of their production, in so far as this is known, suggest that such lesions should not be grouped together indiscriminately.

His systematic observational approach is further illustrated by the later statement that ‘... indiscriminate hippocampal abnormality is not manifestly associated with epilepsy; the link is only between hippocampal sclerosis and epilepsy, and failure to make this distinction has tended to confuse the issue. It is more pertinent to ask, therefore, whether this sclerosis is found in patients who are not epileptic’ (Margerison and Corsellis, 1966).

In this often referred to classic article, together with EEG specialist J.H. Margerison (1922–1970), Corsellis further delimited the spectrum of Ammon’s horn sclerosis in temporal lobe epilepsies by extensive clinicopathological correlations using autopsy material (Margerison and Corsellis, 1966). His studies highlighted the fact that Ammon’s horn sclerosis appears as a spectrum of neuronal loss and gliosis with significant clinical differences related to certain lesional patterns (Blümcke et al., 2007). Among the important findings, ‘the distinction between patients with a [classical] Ammon’s horn sclerosis and those with a lesion confined to the end folium was the age at which the first seizure occurred’, a finding already illustrated in 1957 (Fig. 3).

Corsellis had stated that his post-mortem findings should be identical to Ammon’s horn pathology in surgical epilepsy specimens, although the systematic examination of surgical material at that time was just beginning. ‘When, however, an adequate histological examination has been possible, the Ammon’s horn has often shown a classical sclerosis which is indistinguishable from that seen in post-mortem material’ (Corsellis, 1957). The 1966 paper then mentioned that ‘although end folium sclerosis has not yet been reported in lobectomy material, it has ‘occasionally been seen by J. A. N. C. in specimens removed by Mr Murray Falconer’ (Margerison and Corsellis, 1966). Somewhat earlier, in 1964, Corsellis reported with Falconer and Serafetinides on one of the first large surgical epilepsy series (Falconer et al., 1964), and an additional review on epilepsy pathology appeared in 1970, summarizing the available contemporary data (Corsellis, 1970). Interestingly, many references to the German neuropathology literature are found in Corsellis’ works. Probably, this relates to three facts: Corsellis had lived in Germany for a while, he spoke German (Janota 1995; D. Janz, personal memory) and he was influenced by his mentor Professor Alfred Meyer, who had escaped from Nazi Germany to London (Meyer, 1988). This observation seems quite important, since German-Austrian researchers had built a broad body of studies on histological findings in epilepsy between 1890 and 1950 (Kasper et al., 2009), which remained uncited by most Anglo-American authorities (e.g. Wilson, 1935). J.A.N.
Corsellis notably had an ongoing close view on the clinical context of his findings. With respect to epilepsy, he noted:

Many reports, moreover, point out that the abnormalities tend to lie, or to be at their most severe, in the limbic part of the lobe. The same reports have also stressed, that the outlook for the patients is… better when these deeper areas are included in the resection…; on the other hand [others] have emphasized that fits may also stop after removal of histologically normal tissue and [have] proposed, like Bailey and Gibbs (1951), that the effectiveness of the operation could be due to interruption of the appropriate neural circuits…; for obvious reasons, relatively little of what is known about these pathways has come from investigations of the human brain… this will provide work for the future. (Corsellis, 1970)

The pathology of status epilepticus

Whether epileptic seizures per se and severe seizure manifestations such as series of attacks and status epilepticus lead to neuronal damage was a matter of controversy for a long time. Almost no systematic studies had been carried out preceding Corsellis' efforts. In their contribution to a special Advances in Neurology volume on status epilepticus,Corsellis and Bruton (1983) summarized their experience from a series of 290 autopsy cases. Fifty-two (18%) had a history of one or more episodes of status and 20 (7%) had died in status. Here, they emphasized the obvious differences between children and adults. In children, usual findings were bilateral severe hippocampal neuronal destruction (mainly affecting Sommer's sector), significant cerebellar injury severely affecting Purkinje cells and leading to a glial reaction, and different degrees of thalamic and neocortical damage, which in severe cases were described as ‘almost complete erasure of cortical nerve cells, particularly in the middle cortical layers’. In adults, the general microscopic appearance of the brain was reported to be much less severe and often, evidence of acute damage after status was not present. In their conclusion, they noted: ‘It does not seem possible to go further than this on the available data, and for obvious reasons, relatively little of what is known about these pathways has come from investigations of the human brain… this will provide work for the future. (Corsellis, 1970)

The recognition of focal cortical dysplasia

D.C. Taylor recalls the order of events leading to the classical description of ‘focal dysplasia of the cerebral cortex’ in 1971 by Taylor, Falconer, Bruton and Corsellis:

In 1965 I [DC Taylor] started work with Falconer on a thesis that temporal lobectomy would improve the lives and reduce the psychopathology of some of those who were relieved of their seizures by it. I was making a very close study of 100 consecutive cases for my MD (PhD) thesis. I was interested in brain/behavioural correlations and in the effect of surgery on the subsequent lives of Falconer’s patients up to 25 years after surgery. Here was an opportunity for a psychiatrist to study brain/behavioural relationships as well as study a therapy that was radical and instant. The nature of the lesions was clearly going to be of crucial importance. It was uncertain what factors were going to matter, and since I wanted to know everything there was to know about these patients I was reading everything in the notes, including the neuropathology reports. These reports regularly used similar terms and language to describe what was seen and a conclusion would be drawn. They broke down into relatively few groups, and it soon became possible to follow a description of something outside my expertise. But there were some accounts in which the pathologists had had
difficulty in expressing themselves; they had groped for categories, but clearly none had fitted. No single neuropathologist had had the chance to see more than one or two of these lesions; and there was nothing in the books to guide them. I came upon these descriptions in the notes that clearly mystified the neuropathologist at the time (from 1951 onwards). It was only as I read my way through the Pathology reports of the remaining sets of notes that I could see the recurrences in the words used. I read the details and saw these. I took them to Corsellis. He was very well educated and also German speaking on account of the pre-eminence of German neuropathology.

Looking retrospectively, I could see that these stumbling accounts were describing similar material. Dr. Corsellis listened and then sought out the relevant specimens; that were examined at one of the meetings held regularly between the surgical team and Corsellis. He found the original slides and told me they were indeed similar but a lesion unknown to him. They were often so hard to detect that we assembled a montage of 16 gyri and sulci with some other pathology, or none, or one of ‘these’. These montages were taken by Corsellis, sometimes with me, to various neuropathology meetings. We showed them and asked for guesses or knowledge of these things. No one ever mentioned that they knew this type of lesion, but helpful colleagues invariably could pick out the abnormal four. They were unsure why they were abnormal—‘perhaps because of something like tuberous sclerosis’?

After taking the photomontages of the lesions we saw (mixed in with other brain samples) to Neuropathology meeting after meeting in the UK and the Continent for two years, we wrote up our findings. Corsellis kindly gave me the lead name. He was generous with the paper insisting that it was my work that had raised the issue, ‘discovered’ it. He also had offered me a career in Neuropathology, but it was not my scene. It was Fred Andermann who first used my name for it. In our first formal presentation of the subject, we playfully styled it ‘tuberoid pseudosclerosis’. We may yet prove to have been prescient rather than wrong. Corsellis was most generous, giving priority of authorship to the young enthusiast. A kindly act deserving of wide emulation.

With the publication of ‘Focal dysplasia of the cerebral cortex’ in 1971 a new entity was born. What was new was that these lesions were exquisitely located where they were predicted to be only by EEG localization till the Path turned them up. Also, when the lesion was removed the epilepsy stopped (usually). ‘Cause’ was thus established for that lesion, in that locus. Only since then has the issue of these lesions come to general attention. Now they can be scanned! (D.C. Taylor, personal memory)

Contributions and influence on research on the pathology of psychosis

Aside from his better known work on epilepsy, Nick Corsellis made outstanding contributions to the pathological understanding of psychiatric disease through his own research and the encouragement he gave others (Bruton, 1987). Although for the last part of his official working life, he held the chair of neuropathology at the Institute of Psychiatry, he did most of his work at the department he established at Runwell Hospital.

Runwell Hospital (Fig. 4) was an unusual institution in that it was an area mental hospital located in a somewhat rural part of Essex, near the small town of Wickford, ∼30 miles from the centre of London. One would not have expected it to be a particularly academic centre, and it did not have strong connections with either the University of London or Cambridge, which included the nearest medical schools, but somehow it ‘punched above its weight’ in research. Amongst others, Dr Weil-Malherbe established a neurochemical laboratory there, and later became Head of a Laboratory at the US National Institute of Mental Health. Dr Ashley Robin, a psychiatrist, wrote a significant critical monograph on Lessons of Leucotomy. And perhaps most significant of all, Corsellis established the Department of Neuropathology, which between about 1980 and 1994 acted as a focus for neuropathological investigations of psychosis. The influence of this department is difficult to underestimate. It was one of the few departments of neuropathology located within a mental hospital and therefore had access to brain material. This came from patients dying within the hospital, but also from an active collaborative network with coroners (medical examiners) offices in the county of Essex, and in collaboration with clinical colleagues, who supplied brain material from other hospitals, in this case from Shenley Hospital to the north-west of London. In 1962, Corsellis published a Maudsley monograph on Mental illness and the ageing brain (Corsellis, 1962), a systematic and comprehensive survey of the prevalence of Alzheimer type changes in senile dementia, which up to that time had been a relatively neglected problem. In the course of this work and later, he did much to introduce rigorous quantitative approaches to the assessment of neuropathological change. He returned to Runwell in his retirement and it was here and maybe at this time that he made some of his most important contributions.

I collaborated with J.A.N. Corsellis and his co-workers from 1974 to 1994. At this time I was Head of the Division of Psychiatry at the Medical Research Council Clinical Research Centre, at Northwick Park. I was able to interest Corsellis in psychosis; previously he had always insisted that the brains that he had collected from patients with schizophrenia in the hospital were the best controls he had. He was therefore sceptical at first. Initially this collaboration consisted of occasional visits and discussions about how to approach the problem. Corsellis had written an adventurous and thought-provoking chapter on ‘Psychoses of obscure pathology’ for the third edition of ‘Greenfield’s Neuropathology’, including what was known at the time about the schizophrenic psychoses (Corsellis, 1976). He was thoroughly familiar with the early German literature from Alzheimer onwards, and took a generally sceptical view of the various claims. Interestingly, the chapter was omitted from the fourth edition, published in 1984 and of which he was a co-editor, but was subsequently reinstated in later editions, and provides an instructive contemporary archive of evidence and hypotheses.
In 1976, myself and colleagues had shown in the first computerized tomography study, which the lateral ventricles of patients with chronic schizophrenia were enlarged relative to an age and pre-morbid occupation matched control group (Johnstone et al., 1976), a finding that has turned out to be perhaps the best replicated neurobiological correlate of the disorder. The finding re-activated interest in the neuropathology, and stimulated collaboration with the Runwell Department. When the findings of the initial study had been consolidated (Johnstone et al., 1978) and their implications discussed in the context of neurochemical and pharmacological findings (Crow, 1980), Corsellis suggested a systematic study of a set of brains in the Runwell collection. They used the brain weights and coronal photographs that had been taken systematically at the level of the inter-ventricular foramen in the collected material. After considerable work on the reliability of the measures and their statistical analysis, the paper was published (Brown et al., 1986) with an alphabetical authorship; Rosemary Brown, Corsellis’ outspoken senior technician, responsible for brain collection over many years, was first author. The paper established that ventricular enlargement could be detected in post-mortem material, that the brains were lighter (by 6% in this series), and that such changes as there were in cerebral cortex were most marked in the parahippocampal gyrus. We discussed a degree of asymmetry in the findings in schizophrenia by comparison with affective disorder (the main control series in this study), but did not emphasize this in the abstract.

Systematic post-mortem studies of psychosis were now under way. They were dependent on the survival of the Runwell Department, but as a result of changes within the health services (long-stay psychiatric institutions were under critical scrutiny and in process of being closed); the future of the Runwell Department was in doubt. Corsellis himself was now well into his retirement and of poorer health. He took a less prominent role, but by good fortune Clive Bruton (who had trained as a neuropathologist with Corsellis at Runwell years before, but had spent most of his professional life as a general practitioner in Birmingham) was able to take on increasing responsibility for the histopathological assessments. Corsellis and Bruton had contrasting personalities. Corsellis had a wry sense of humour, and observed human society with gentle scepticism, and as if from a distance; Bruton was more sanguine, enjoyed greyhound racing, bawdy theatre and good living. They understood each other well. Both were enthusiastic that research on psychosis should go forward, and Bruton sustained the programme through to the early 1990s. For some of these years (perhaps 1988–1993), the Runwell Department was financially supported by the Medical Research Council through the Division of Psychiatry of the Clinical Research Centre at Northwick Park. This was due to the support of the Director, Sir Christopher Booth and the Administrative Director, Keith Kirkham. At Northwick Park, clinical research progressed over these years due to the devoted efforts of Eve Johnstone and David Owens, ably assisted in neuropsychological assessment by Chris Frith, in documenting the in-patient population of Shenley Hospital. In due course a number of patients died, and again due to the persistent efforts of these clinical colleagues, a high proportion were included in the next post-mortem series which is perhaps the largest and most thoroughly investigated study yet reported. The major neuropathological findings were presented by Bruton et al. (1990). The discussion of this article reflects the resolution of considerable differences of opinion between the authors in the conclusion that such pathological findings as gliosis and vascular change as were present did not account for the morphological deviations e.g. ventricular size and shape anomalies. Another finding to emerge from the clinical assessments was that negative symptoms were correlated with brain weight and length (Johnstone et al., 1994).

To investigate ventricular enlargement further, Corsellis suggested that the ventricles of the fixed hemispheres should be filled with radio-opaque material and X-rayed from the lateral aspect. This led to the rather striking finding that proportional enlargement was greatest in the temporal horn and selective to
the left hemisphere (Crow et al., 1989), a finding that has been echoed in some later MRI studies (Narr et al., 2001). This study led on to concepts of pathophysiology (Crow, 1997) and aetiology (Crow, 2000) that remain topics of debate (Crow, 2008). Other contributions came from the Runwell Department and Corsellis’ influence. The hypothesis that gliosis was systematically related to schizophrenia, made by Nieto in Minkler’s Textbook of Neuropathology (Nieto and Escobar, 1972), was ruled out in two investigations (Roberts et al., 1986, 1987). On the basis of Bruton’s Maudsley Monograph on the histopathological findings in temporal lobe epilepsy (Bruton, 1988) came a study relating to the psychiatric sequelae of the differing types of lesion (Roberts et al., 1990). These studies illuminated the problem from an entirely different aspect.

This is an account of the work that developed from the collaboration between the Division of Psychiatry and Professor J.A.N. Corsellis at the Department of Neuropathology that he founded at Runwell Hospital. I, T.J. Crow, have warm recollections of the collaboration with Corsellis and Bruton, who I regard as significant figures in my life. I would like to think that the influence of that collaboration is reflected, along with subsequent work in Oxford, in the chapters that my collaborator Margaret Esiri and I wrote on ‘Psychiatric diseases’ in the seventh and eighth Editions of Greenfield’s Textbook of Neuropathology, as successors to the chapter on ‘Psychoses of obscure pathology’ in the third edition, written by Corsellis.

Other research fields

Earlier in his career, Corsellis contributed to the hypothesis concerning the transmissibility of dementia, i.e. the complex of Creutzfeldt-Jakob Disease (Corsellis, 1979, 1986). He repeatedly published on the cerebral sequelae of boxing, i.e. ‘dementia pugilistica’ (Corsellis et al., 1973; Corsellis, 1989). The seminal paper published in 1973, with Bruton and Freeman-Browne, entitled ‘The aftermath of boxing’ drew attention to the frequency and severity of gross brain damage of those subjected to levels of brain trauma, which previously had been thought innocuous, and fuelled the intense and continuing debate on the medical consequences and ethics of boxing as a sport (Corsellis et al., 1973).

Furthermore, Corsellis was interested in resolving certain methodological problems inherent to neuropathological techniques. This is exemplified by his work on the reliability of cell-counts (Corsellis et al., 1975; Miller et al., 1984). Together with his young colleague Miller, he was developing a computer-based neuronal counting method allowing for systematic investigation of neuronal populations (Corsellis et al., 1975). In another paper, he developed a strategy for investigating the territorial incisura: ‘The present report therefore describes first a post-mortem technique for the study of the tentorium from below, and secondly the individual variation in the size and shape of the tentorial opening that has been revealed by the use of this method’. The striking interindividual anatomical variation and its implications for trans-tentorial herniation is discussed here (Corsellis, 1958).

Contributions to and editorship of Greenfield’s Neuropathology

As already mentioned, J.A.N. Corsellis took editorship for two volumes (the third and fourth editions) of Greenfield’s Neuropathology, the pre-eminent textbook of neuropathology. Notably, Corsellis was acknowledged as the source of many photographs from the early editions (Greenfield et al., 1958; Blackwood et al., 1963). This textbook had been founded by Joseph Godwin Greenfield (1884–1958) and represented the first concise English summary of clinical neuropathology following the foregoing ‘Pathology of the nervous system’ (Greenfield and Buzzard, 1921). In the first (1958) and second (1963) volumes, the chapters on epilepsy had been authored by Professor Alfred Meyer (Greenfield et al., 1958; Blackwood et al., 1963). Meyer was leading the neuropathology service at the Maudsley and was one of the few specialists on epilepsy pathology at the time (Daniel, 1999). He had learned many aspects within the Munich School of Neuropathology, from Walter Spielmeyer. Spielmeyer, the most outstanding figure in German neuropathology (Corsellis, 1991) had authored an important book entitled ‘Histopathologie des Nervensystems, Allgemeiner Teil’ (Histopathology of the nervous system—general part) (Spielmeyer, 1922), and Greenfield later had encouraged Meyer to translate this seminal work into English, but he refused (Meyer, 1988). Due to great support by Spielmeyer, Alfred Meyer moved to the Maudsley after leaving Nazi-Germany in 1933 (Peiffer, 1997, 1998). He built a congenial team with specialist laboratory scientist Elisabeth Beck, producing outstanding papers, including epilepsy pathology after establishment of an epilepsy surgery programme by Murray Falconer in 1950 (Meyer et al., 1954; Meyer and Beck, 1955). Meyer, standing in the German tradition of neuromorphology, became a leading neuropathologist and a scientific mentor to Corsellis, who himself had spent a period with Scholz in Munich (D. Janz, personal communication). Not surprisingly, Corsellis took over contributions to the sections on epilepsy in the following editions of ‘Greenfield’s neuropathology’ (in cooperation with Professor Brian Meldrum) (Blackwood and Corsellis, 1976; Adams et al., 1984). These chapters closely follow the structure chosen by Alfred Meyers’ contributions to the first two editions. It is reasonable to assume that it was Meyer who offered Corsellis the opportunity to make these contributions. The 1976 preface states that

…Professor Meyer and Professor Russell felt that the preparation of a new version should be passed to the next generation of British neuropathologists, guided by Dr. Greenfield’s colleagues and successors at the National Hospitals, Professor McMenemey and Professor Blackwood. …Lastly, because of Professor McMenemey’s much regretted retirement, Dr. Corsellis has joined…to assist in editing the present volume. (Blackwood and Corsellis, 1976)
Corsellis also contributed important chapters on ‘Ageing and dementia’ (third and fourth editions) and ‘Psychoses of obscure pathology’ (third edition).

Overall, it seems that J.A.N. Corsellis continued the tradition and spirit of clinical neuropathology exemplified by Dr Greenfield. Both Greenfield and Corsellis were ‘primarily pathologist(s), but never lost sight of ... clinical training’ (Blackwood and Corsellis, 1976).

### The Corsellis Collection brain bank

Corsellis’s name is closely linked to a large collection of brain specimens from various diseases, which he built starting in the early 1950s. This brain bank was the centre of an official investigation, after a patient’s wife realised that her husband’s brain had been retained for research without her consent (Butcher, 2003). In 2001, Jeremy Metters (Her Majesty’s Inspector of Anatomy) was asked to investigate the circumstances; he showed that the collection complied with the regulations that applied at that time, the majority of the brains being Coroner’s cases with permission for the retention of the brain for further studies (Metters, 2003). The Metter’s report (‘Isaac’s report’) led to the creation of the Human Tissue Act in 2004, replacing the Human Tissue Act of 1961, the Anatomy Act 1984 and the Human Organs Transplants Act 1999. The Corsellis Collection now holds a license under the Human Tissue Act as an archival brain collection. As stated in the report ‘discoveries of major clinical importance have only been possible through research based on the number and diversity of [this] collection. Professor Corsellis pioneered the concept of research based on brain archives and collections’ (Metters, 2003).

Furthermore,

In Runwell ... a post-mortem [including brain examination] was almost always carried out for diagnostic reasons; ... [Corsellis] retained those that were of diagnostic interest [as well as] ‘control’ brains, when neither the patient’s history nor the post mortem findings indicated any disease. As early as 1953, the Medical Research Council awarded Corsellis a grant for his research on the collection. Later ... the value of the collection for further research and teaching was recognized. In this way an accumulation of brains ... evolved over the following decades to become an invaluable research archive; ... an increasing number of brains were referred to him for his expert opinion. Corsellis devoted his life’s work to research on the collection. When [he] retired from his academic post at the Institute, he continued to develop the collection and his research based on it. After [his death] in 1994, the collection continued under the leadership of Dr Clive Bruton, who had joined the team in 1968. (Metters, 2003)

Dr Bruton’s death in 1996 coincided with plans to close a large part of Runwell Hospital. After announcement that the collection was available, the West London Mental Health Trust together with the Department of Psychiatry at Imperial College, recognizing the unique value of this collection, transferred it to the West London Mental Health NHS Trust, St Bernards site, West London, in 1997. It is now a tissue bank for research worldwide. Currently the bank consists of approximately 5000 samples in formalin, and additional samples held in the form of paraffin-wax and celloidin blocks, and a substantial amount of histological slides. In addition, the collection holds many thousands of neuropathological reports, medical records and neuropsychiatric review notes related to the samples. Currently there are parallel studies to review the clinical diagnoses of many of the cases included by modern criteria. The bank is in the process of optimizing protein and DNA extraction from the different tissue types held, allowing samples from the collection to be used for more than simply neuropathology projects. These molecular techniques would greatly improve the contribution that the collection could make to neurological research in a way that could not have been envisaged half a century ago, upon its formation.

### Concluding remarks

J.A.N. Corsellis (Fig. 5) was an enthusiast for research into the nature of psychiatric illness, epilepsy and major neurological disease. He facilitated progress without concern for credit for himself.

![Figure 5](https://www.oxfordjournals.org/by-guest-on-october-6-2016)
Both as a person and researcher he and his work, including his collection of brain tissue, had significant impact on the field of neuroscience. He created new and extended existing knowledge concerning neuropathology of many neuropsychiatric diseases. Many of his observations were groundbreaking and are still valid. His enthusiasm for approaching problems of psychiatric disease through brain morphology inspired co-workers and collaborators. Perhaps his most important contribution was as an ambassador, representing neuropathology in academic psychiatry. He was well qualified to do so as he had himself started training as a psychiatrist. He was a penetrating commentator on those issues where he felt his discipline could make a contribution. He was always willing to join in discussions across boundaries and into the more psychological and psychiatric fields, areas few fellow pathologists were willing to follow.

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The authors were not able to contact or localize any of Prof. Corsellis family members. If existing, we hope the manuscript is well received. Anyone knowing about important aspects not mentioned in this manuscript is welcome to contact B.S. Kasper.

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