MENTAL CHANGES AS A PRESENTING FEATURE IN SUBCORTICAL CEREBRAL LESIONS*

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LESIONS of the cerebral cortex are generally accepted as a potential source of psychological change, and the difficulties that may arise in distinguishing between one of the psychiatric illnesses at present regarded as idiopathic and one due to a lesion of the prefrontal cortex, the temporal lobe or the posterior parietal region are well recognized. Since there is normally a continual functional interplay between cortex and subcortical structures, lesions in the latter may also be expected at times to produce changes in psychological function.

That such lesions may give rise to gross alterations in consciousness, apart from those due to any general rise in intracranial pressure, has been recognized at least since Foerster (1926) drew attention to them. In 1944 Jefferson elaborated the theme that brain stem structures were important in maintaining consciousness; and Cairns (1952) reviewed his wide experience of such lesions and the changes they may produce in crude consciousness or awareness. These changes do not usually present as psychiatric problems, since the all-or-none way in which consciousness is altered and the accompanying neurological signs indicate their organic basis. However, subcortical lesions also appear able at times to produce more insidious psychological change, and the five cases described in this paper serve to illustrate this point. Such changes have a two-fold interest. In general they demonstrate, for a neuropsychiatry which views the brain as the organ of adaptive behaviour, the complexity and integration of the neurological substrate of mental life. More particularly, they may simulate idiopathic psychiatric illness and give rise to diagnostic difficulties, especially as conventional neurological abnormalities may be absent.

Three of the five cases discussed presented with psychiatric symptoms: one was first thought to be a cortical dementia; while in the fifth, a local subcortical lesion was recognized *ab initio*, but it produced a reversible memory defect of the type associated with a Korsakoff syndrome, and the implications of this were considered of sufficient interest to merit recording the case.

CASE MATERIAL

Case 1. (*R.I. 184607*)

A housewife of 29, previously capable and well-balanced, had a three months history of increasing general incompetence and emotional instability, mainly of depressive type. There was no family history of mental disease. Her domestic situation was unsatisfactory. She looked after her three-year-old daughter and her mother, who had hypertensive heart failure. Her husband, who only sporadically visited the household, had been in the hands of the police and was once more up on a charge of larceny.

Two months before she was seen she had an illness characterized by fever, vomiting and headache. This followed a similar attack in her small daughter, and it had been diagnosed as "food poisoning". The fever had subsided, but some headache and occasional vomiting persisted.

Her sister reported that during the past month her memory had been capricious, and she seemed increasingly uninterested in her family's welfare. She appeared muddled at times. On one occasion she had put a pudding into the oven on top of a meat pie so that they had become mixed and cooked together, and had served them without comment. On another she

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had retired to bed at mid-day for no reason, and had refused to get up until her sister made her. In the past ten days she had had two "faints", with sudden falling and probably loss of consciousness.

On examination there were no abnormal signs in the central nervous system. In particular her optic discs and fundi were normal. The most striking feature was her incongruous behaviour. At times she would answer questions promptly and correctly, at others she would pause and look in a puzzled way round the room as if searching for the answer. She would smile or laugh for no reason, and on one occasion broke down and wept for no apparent cause. She performed various motor tests accurately, but occasionally perseverated and repeated inappropriately the action of a previous test. She was orientated for time, place and person, and was aware of the mistakes she made in tests and of the incidents recalled by her sister; but her reaction to them was curiously apathetic.

Despite the negative findings, her two unexplained faints and some slow wave abnormality in the occipital region in her electroencephalogram, suggested the need for further neurological investigation. Lumbar puncture gave a normal C.S.F. pressure, but a protein of 100 mg. per 100 ml. Following this she became obviously confused and had an attention defect in the left half visual field, and a suggestion of left hemiparesis. Ventriculograms showed a large space-filling lesion in the right basal ganglia, which proved on biopsy to be a glioblastoma. She was referred for deep X-ray therapy.

Comment. This lady presented as a psychiatric problem. Her symptoms were at first thought to be an anomalous reaction to her domestic worries; though her later incongruity of behaviour led her doctor to consider a schizophrenic illness—a diagnosis certainly rather suggested by her behaviour on first examination at hospital.

Case 2. (R.I. 96382)

A housewife of 38, who also did secretarial work, had a history of two months abnormality of behaviour. There was no family history of mental illness. Her family had always considered her rather emotional and prone to exaggerate, but she had done well at school and at work. She had been married for five years and was very disappointed that she had no children. Her husband worked away from home and only came back at weekends. She resented this.

Her behaviour change was marked, and its onset was associated by her husband with an attack of mild influenza. It was characterized by sudden emotional upsets on the most trivial provocation, when she would become angry or tearful. She would also at times suddenly leave what she was doing and wander off, with no clear memory afterwards of where she had been. Thus during a cycling holiday with her husband, he had gone on ahead down a hill and then waited at the bottom. When she did not appear he went back to find her bicycle propped up at the roadside. After searching for some time he met her walking back to the road across some fields. She would give no explanation for this, and said she could not recall where she had been. Again, one morning she refused to come down to breakfast, although she had got up and started to dress in a normal manner, but lay half dressed on her bed and refused to reply to her husband's questions. He went down and she appeared later and had no recollection of the incident. Other similar incidents had occurred; but in between her behaviour had also been childish and over-emotional. Her husband regarded it as quite different from her usual self. However, she was able to carry out her household duties and her general intelligence and memory seemed unimpaired, apart from the amnesic episodes mentioned.

She had twice complained of an attack of tingling in her lips with cramp in her feet. On these occasions she was emotionally upset and breathing deeply, and the symptoms were considered to be due to hyperventilation tetany. She slept poorly and for a month had taken barbiturates sporadically. Apart from this there were no physical symptoms. She herself had complained of insomnia and constantly worrying about nothing, and it was for this that she had consulted her doctor.

Examination by her own doctor and a medical specialist had shown no physical abnormalities. Some three weeks later, on the day of her admission to hospital, she had refused to get up to breakfast, but had later appeared looking dazed and had been taken back to bed again. During the morning she fell out of bed and there was some question of her having had a fit, but this was never clearly established. She was found in a stuporous condition at mid-day, and from then until her death three months later she never regained full consciousness.

No localized abnormalities were found in the nervous system or elsewhere. At times her eyes were open and she appeared to follow movements, but she responded only to noxious stimuli such as pinprick, and later was unresponsive and in deep coma. Her electroencephalogram showed a diffuse slow wave abnormality, more marked anteriorly. Her C.S.F. was normal. Burr-hole exploration and ventriculograms also showed no abnormality. She developed pressure sores and a hypostatic pneumonia which provided the *exodus lethalis*.

At autopsy the brain showed a healed meningitis under one burr hole, with a small healed abscess in the brain needle tract. Cortical convolutions were rather flattened, but there was no other gross pathology. Histology revealed some evidence of inflammation with perivascular cuffing in the hypothalamic region and floor of the third ventricle.

Comment. For two months this lady presented with emotional upsets and occasional fugue-like episodes, which were regarded as hysterical, as was her apparent hyperventilation tetany. For the first week of her hospital admission the possibility of a catatonic schizophrenia was considered, but it seemed much more likely despite the absence of abnormal neurological

signs, that she had an organically determined illness, and after her negative ventriculograms a diagnosis of encephalitis lethargica was in fact entertained.

Case 3

An unmarried man of 27, a post-office worker, had suffered for some two years from attacks of acute panic. There was no family or personal history of mental disorder. Initially the attacks occurred only once in three or four months, but their frequency had increased and this had caused him to seek medical advice. He was intelligent and co-operative, and gave a vivid description of his attacks. Quite abruptly and without warning he would feel terrified as if something awful was about to happen. He felt compelled to get home and to his own room as soon as possible. Once there, he would lock the door and bury himself under the bedclothes fearful of the least sound from the outside world. His terror was quite diffuse and there was no fear of impending death. Seen at the beginning of an attack, he was pale and with rapid pulse and dry skin. Each attack lasted for half to three quarters of an hour, and ceased rapidly, though not as abruptly as its onset. No psychogenic factors were discovered. Between attacks he was well and able to do his work; though latterly there was some general apprehension about their further occurrence.

On examination there were slight but unequivocal signs of Parkinsonism. His face was immobile, ocular convergence was defective, and there was bradykinesia and a little cogwheel resistance to passive movement in the left hand. He showed evidence of excessive salivation. Skull X-rays and C.S.F. were normal.

Six years previously he had had a febrile illness which had kept him in bed for three weeks. For ten days of this he now had no clear recollection, and his mother described him as "delirious" at the time. The condition had been diagnosed as severe influenza by his general practitioner.

Comment. This patient was regarded as a post-encephalitic Parkinsonism. The evidence associating his panic states with the Parkinsonian lesion was only circumstantial. The attacks were suggestive of a discharging lesion in Hughlings Jackson's sense, and were reminiscent of true vaso-vagal attacks, though no specific *angor animi* appeared. Similar acute anxiety attacks are seen in post-encephalitic states in association with the sudden attacks of disordered respiration that sometimes occur. However, no evidence of respiratory upset was elicited on careful questioning here. The interval of some years between the original illness and the subsequent symptoms does not exclude a causal connection, since similar intervals are seen in the narcolepsy-cataplexy group of sequels. The general setting of the attacks, the absence of any discernible psychogenesis and their amelioration with phenobarbitone and tincture of stramonium during some months of observation, seemed to justify regarding them as post-encephalitic manifestations.

Case 4 (*S.M.H. 27453*)

A housewife of 59 with no previous personal or family history of mental disorder, was well until the unexpected death of her mother, when she gradually became increasingly depressed and unable to manage her housework. Her family noticed marked memory impairment. She would put household utensils and money carefully away, and then forget where they were. This upset her greatly. When first examined there were no abnormal physical signs, and her symptoms were considered to be a psychological reaction to the death of her mother two months before.

Over the next six months her symptoms persisted and she developed precipitancy and occasional incontinence of urine, and some ill-defined difficulty in walking. Examination now revealed a rather euphoric woman with much emotional lability. There was a marked memory defect for recent events and a poor performance on formal memory tests. There was some nominal aphasia and a suggestion of constructional apraxia. Her optic discs showed no papilloedema. A fine tremor of the outstretched hands was seen, but no limb inco-ordination, dysarthria or nystagmus. She had no true ataxia of gait, but she walked in a shuffling manner and complained of feeling unsteady. Her tendon jerks were brisk and there was a slight cogwheel resistance to passive movement, but no other abnormalities in the central nervous system. Her C.S.F. showed a protein of 90 mg. per 100 ml. but was otherwise normal in content and pressure. Her electroencephalogram showed some generalized abnormality with mixed slow and fast wave (3, 6 and 22 cycles per second) but no paroxysmal activity. There was some poorly developed alpha rhythm which blocked on eye opening.

She was considered to be an early organic dementia, probably a pre-senile cortical atrophy. However, in view of the high protein, lumbar air encephalograms were attempted on two occasions, and as they were unsatisfactory, ventriculograms were done. The burr holes revealed normal supratentorial pressure. There was some enlargement of the lateral ventricles; the third ventricle was normal; but the fourth was distorted and suggested a posterior fossa space-filling lesion.

At operation a haemangioblastoma of the right cerebellar lobe was successfully removed by Mr. J. Pennybacker. Although there was some displacement of the brain-stem and cerebellar tonsils, posterior fossa tension was not raised. For two weeks after operation she was worse mentally and physically. She was confused and disorientated for time, place and person and had gross cerebellar dysfunction. During the next three months, however, she improved rapidly and steadily. On discharge home she had no abnormal physical signs, apart from a

slight nystagmus and clumsiness of right hand movement. She was sensible, co-operative and fully orientated, and her memory both in everyday life and to formal testing was normal. She returned to full household duties and social life, and the improvement has been maintained for the past three years.

Comment. This lady after an initial depressive reaction, presented as a generalized deterioration of higher cortical function. The severe memory defect and the nominal aphasia suggested an Alzheimer or Pick's disease and the slight suggestion of extrapyramidal rigidity seemed to confirm this. The rapid reversal of the dementing process after removal of the cerebellar tumour was striking, and rebutted the view based on the original clinical evidence that she was suffering from an irreversible cortical degeneration.

*Case 5 (R.I. 111669)**

A young man of 22, a farmer's apprentice, was admitted for investigation of headaches and sudden unpredictable sleepiness. After some 18 months observation and treatment he died and autopsy confirmed the clinical diagnosis of a large cystic and solid tumour involving the floor of the third ventricle. Posteriorly it had stretched the cerebral peduncles and the pons was slightly flattened, and anteriorly it abutted on the optic chiasm. The lateral ventricles were large, but there was no evidence of cerebellar or tentorial coning. The tumour had pushed up anteriorly into the third ventricle; the tuber cinereum was largely destroyed and the inferior aspect of the left thalamus was involved.

For a time the tumour had interrupted C.S.F. circulation and had caused a marked rise in intracranial pressure. This was accompanied by a slight left hemiparesis and defect of upward eye movements, and by severe confusion, drowsiness and even coma. His electroencephalogram then showed much high voltage random theta and delta activity, with no alpha rhythm. Ventricular tapping relieved the pressure and the gross confusion and drowsiness cleared for a while. His electroencephalogram now showed some 9 c.p.s. alpha posteriorly. There was no delta or random slow-wave activity, but runs of bilateral synchronous theta occurred.

As a ventriculocisternostomy did not give permanent improvement, the cystic part of the tumour was directly tapped. Shortly after this the patient was alert and co-operative, and would answer questions and obey commands readily. However his memory for recent events was seveiely impaired. He could not remember what he had for his last meal, nor what he had been doing during the preceding few hours. In reply to questions he would confabulate with details of his work on the farm. He described feeding the pigs and milking the cows, and could be led on to elaborate this, giving the names of the various beasts and their idiosyncracies. He failed in simple memory and retention tests, but would usually confabulate an answer, and would not admit that he could not remember. However, his digit span was 7 forwards and 5 backwards; and he gave the year, the day of the week and the date correctly (he had just been reading the paper). He admitted he was in hospital with doctors and nurses around him. When the discrepancy between this and his previous statements was pointed out, he said he had been out on the farm just before he came in.

As more generalized confusion and drowsiness recurred, the cyst was again tapped. Following this, he again became fully orientated and his confabulation ceased. As the cyst filled up again the Korsakoff state reappeared and then passed into drowsiness and confusion. The sequence was repeated on several occasions.

Comment. This case never presented any diagnostic difficulty. He was of interest as showing that one mechanism involved in the registration and organizing of memory appears to lie in the grey matter in the floor of the third ventricle. At the relevant times the patient showed in a setting of general alertness the two features of a Korsakoff syndrome, amnesia and confabulation. He was unable to retain memories of events occurring at the time though he evidently perceived them, and he would fill in the gaps with confabulated material. This was always part of his past experience and was never invented. The difficulty appeared to be one of organizing past experience in its correct temporal setting—a severe but partial disorientation for time.

Such a disability has been noted previously in lesions in this situation, both in third ventricular tumours (Williams and Pennybacker, 1954) and in tuberculous meningitis (Williams and Smith, 1954) where inflammation and exudate are maximal around the base of the brain. Moreover, histological changes in classical alcoholic Korsakoff's syndrome have been found most consistently in the hypothalamic region.

Discussion

Localized subcortical lesions occurred in basal ganglia, hypothalamus or brain-stem in all these cases and in four of them presenting symptoms were in the psychological sphere. In the initial stages they did not involve gross changes

* This case was discussed in detail by Williams and Pennybacker (1954, Case 4). Here it is mentioned only to illustrate the occurrence of confabulation without general confusion, and the EEG changes associated with raised intracranial pressure.

in consciousness, though in some cases these supervened later. Early changes were insidious, but were quite evident to relatives, friends and often to the patients themselves. Increased lability and incongruity of affect, acute anxiety, depression and apathy were all seen. Some intellectual change was also noted in three cases, in one amounting to a mild dementia. The changes are not easily summarized, but they resulted in a breakdown of normal adaptive behaviour sufficient to call for medical advice. In the two cases with no abnormal physical signs, episodic disturbance of intellectual functions and a perhaps anomalous personality change raised the suspicion of an organic lesion, but it was only the findings of adjuvant tests that gave a definite lead.

Any space-filling intracranial lesion may produce a general rise in intracranial pressure. A stenosing or inflammatory lesion if strategically placed may have the same effect by interfering with C.S.F. circulation. Such pressure changes will have widespread effects on cerebral function, and will be of no localizing value in attempting to assign specific functions to particular sites. It is therefore important to exclude this pressure factor in the cases we are considering.

The physical evidences of this—papilloedema, raised C.S.F. pressure at lumbar puncture, tense intracranial contents at operation, and characteristic electroencephalogram pattern—were not present, except in Case 5. There, as has been pointed out, it was at times when the general intracranial pressure had been operatively lowered that the symptoms of particular interest to us emerged. Moreover, the typical mental changes of raised pressure—a rather generalized cortical dysfunction with marked loss of responsiveness even to a level of deep coma—were also not part of the initial picture in these cases. Indeed, Case 5 illustrates well the diagnostic value of the type of mental change observed. When his intracranial pressure was in fact raised, the presenting psychiatric picture was one of drowsiness or coma; when pressure was reduced he became alert and readily accessible, though confabulation and pseudo-reminiscence were easily elicited. There is therefore nothing to suggest that the symptoms observed in these cases were due to general pressure changes, rather than to the specific site of lesion.

Psychiatric symptoms may at times arise during an organic illness and be unrelated to it in a specific causal sense. In these cases, this seems unlikely. In all of them the changed behaviour was clearly recognized by relatives and represented a departure from their usual method of dealing with life's difficulties. In three, treatment directed to the organic lesion relieved the symptoms, even though in one (Case 4) they had seemed at first to be occasioned by emotional shock.

Previous descriptions of the effects of subcortical lesions on mental functions have generally emphasized a crude change in consciousness, loss or gross clouding of consciousness, drowsiness or coma. Foerster (1926), Reichart (1929), Cairns *et al.* (1941) and Jefferson (1944) have all described such changes. More recently, the defining by Magoun (1950) and his colleagues of the reticular formation in animals—a band of tissue lying between the main afferent and efferent pathways, and extending from the thalamus through the brain-stem to the medulla—of which stimulation produces a diffuse activation of the cortex and destruction a condition akin to sleep or coma, has renewed interest in the possible neurological mechanism of such symptoms in man. However, no convincing evidence is yet available for any homologous well-defined "subcortical activating system" in man; though the work of Jasper (1954) and others in correlating the electrical activity of limited areas of the thalamus with diffuse

cortical changes and accompanying alterations in mental state, seems to point that way. Less convincingly, French (1952) has suggested that in three cases with prolonged coma, autopsy findings supported a lesion of some such mechanism, and Cairns (1952) much more tentatively raised the possibility in some of his cases.

In both these instances the mental changes were in the sphere of crude consciousness or awareness, though Cairns specifically mentioned more circumscribed changes in memorizing: as have others (referred to above, see Case 5), in discussing lesions in the region of the third ventricle. In the present cases mental changes were more subtle and were unaccompanied at the relevant times by any general confusion or loss of awareness. They did not suggest involvement of any all-or-none mechanism for general wakefulness or awareness.

The personality changes in adults and the more striking psychopathic behaviour in children, without neurological abnormality, which may follow von Economo's encephalitis, where basal grey matter and brain stem tends to be maximally involved, may also be examples of dysfunction of these subcortical areas. The difficulty in accepting this argument without reservation, is the known occurrence in some cases of changes in the frontal lobes as well.

Whether the changes noted in our cases represent the effect of simple interruption of some fixed anatomical pathways, or (as I think more probable) the result of abnormal neuronal discharge actively interfering with normal cortical function, they seem to imply a more elaborate functional interrelation in the mental sphere between cortex and subcortex than has previously been emphasized; and one which allows localized subcortical damage to produce insidious mental changes.

The presence of an organic brain lesion was finally established without doubt in all five cases. In four, however, an alternative psychiatric diagnosis was considered for some months. Such lesions may therefore lead to diagnostic difficulties. Of greater interest and importance is the light that they may shed on the neurological basis of psychological function. The mental symptoms observed were due directly or indirectly to involvement of limited areas of subcortical tissue, in these cases by structural organic damage. However, the function of these same areas may be affected by transient and reversible lesions; from ischaemic or toxic processes or even from unusually intense bombardment of otherwise normal synapses in the region. When, therefore, such symptoms are seen in an apparently psychogenic setting the possibility must be considered that here also similar neurological mechanisms are involved. This may have implications both for the origin of symptoms and for their treatment. It should be emphasized, however, that this does not preclude psychological stimuli acting via cortical mechanisms as a primary factor in such disturbances of mental function, since cortico-subcortical connections are probably as abundant as those in the reverse direction. Indeed, it is the close similarity of symptomatic end-results from either primary psychological factors or organic subcortical lesions that emphasizes the need both for clinical vigilance and for renewed consideration of cerebral function in mental disease.

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