Huglins Jackson (1932) said about memory "Remembering in the sense of having again is somebody having again." Memory for him was subjective. The doctrine of psycho-physical parallelism, to which he was committed, did not allow for the possibility that memory was "a physical system by which there is made a record or representation of certain past events" (Young, 1965). Young, whom I have quoted, goes on to say "It is in the nature of records to be consulted when future action has to be decided on. Such consultation in man is made by the agency that each of us rather enigmatically calls 'I', but the record is a physical system and could in principle be consulted by anyone." This is the point of view that I shall adopt. It extends the range of observation to learning in animals. We need not ignore the feats of memory observed in insects or birds, or in the octopus. According to the doctrine I have adopted, the neurologist and the psychologist should be approaching the investigation of memory and its disorders from two sides in the hope of meeting, and to this end they should collaborate. Collaboration requires communication. Here difficulties arise over terminology. We have been often warned against the dangers for the neurologist of borrowing psychological terms for neurophysiological interpretation, and vice versa. Yet it seems impossible to avoid this, if hypothesis is to be fruitful in the field of what has now come to be known as neuropsychology. I shall accept the implications of this term.

I shall consider in this lecture only such cases in which, as the effect of organic brain damage, proven or presumed, there may be observed disorder of memory accompanied by little or no general intellectual impairment. As a rule there is none, and the patient despite his lowered capacity for remembering recent events, even though this is grossly impaired, is able to think and reason clearly within the limits imposed
by his defective memory. Associated with this there is retrograde amnesia (R.A.).

This amnesic syndrome may be observed in many different diseases. I shall not attempt to cover the whole field, but shall select examples that may form a basis for discussion of the psychological and neurological problems involved.

Clinico-pathological Correlations

In certain instances the syndrome is associated with proven localized brain damage. Of these, Korsakoff's psychosis provides the longest known example. The title should be reserved for cases in which the memory disorder appears as a sequel of Wernicke's Encephalopathy caused by thiamine deficiency. The lesions almost always involve the mammillary bodies and adjacent areas (Brierley, 1961), though recent observation suggests that bilateral damage to the medial dorsal nuclei of the thalamus is of critical importance (Victor, 1964). The cerebral cortex is microscopically normal (Delay et al., 1958). In Korsakoff's psychosis there is R.A. and severe impairment of recent memory, without clouding of consciousness, and with good retention of skills and knowledge ante-dating the R.A. Liepmann's (1910) patient, for example, with a persistent R.A. of 25 years, and preservation only of immediate memory, played chess well. As will be noted later, Korsakoff's psychosis, which has been intensively studied by Talland (1965), stands a little apart from the other amnesic syndromes, in that, besides the memory disorder, there is generally some evidence of other intellectual impairment, and of personality disorder, though these changes are relatively slight.

The effects of bilateral temporal lobectomy in man are of outstanding importance. Most of these operations were done for schizophrenia. Milner (1959), however, reported a case in which the operation was performed for the relief of intractable epilepsy in a patient whose pre-operative mental state was normal. After the immediate effects of the operation had worn off he was able to remember very little of the experiences of the past 12 years. His memory for more remote events was intact. There was no evidence of any general intellectual loss, nor any restriction of digit span, but there was a gross defect of recent memory. This persisted, though there was shrinkage of the R.A. Similar data have been reported in a few cases of unilateral temporal lobectomy, that of Dimsdale, Logue and Piercy (1963) being an especially well-documented example. Ablation of the hippocampus appears to be the essential lesion.

A comparable clinical picture of memory disorder has been recorded by Victor and others (1961) in a patient proved at post mortem to have extensive infarction involving the hippocampus on both sides from
occlusion of the posterior cerebral arteries. There was severe impairment of recent memory and a patchy R.A. for two years. Skills and knowledge acquired during the years before this were well preserved. The patient was still able to play bridge adequately and actually taught his nephew to play solitaire. The case of Glees and Griffith (1952), though less well documented on the clinical side, provides a further example. In this case the sudden onset of the illness was consistent with infarction, and at post mortem 15 years later, cystic lesions were found destroying the hippocampus and adjacent areas on both sides. The corpora mammillaria were intact.

It has long been recognized that an amnesic syndrome may follow recovery from status epilepticus. Delay and others (1965) have recently recorded such a case with gross defect of recent memory and R.A. dense for 3 years, and severe for 24 years, intellectual function apart from the amnesia being normal. The patient died from an unrelated cause one year later, and examination revealed severe anoxic damage in both hemispheres involving the hippocampo-mammillary circuit and thalamus.

There is therefore firm evidence for the conclusion that bilateral lesions of certain parts of the diencephalon can result in a permanent disorder of memory comprising a long R.A. with severe impairment of recent memory, without other intellectual impairment. The rôle played by damage to the corpora mammillaria is less certain. Bilateral temporal lobectomy, including hippocampus, produces the same clinical picture. It appears that a unilateral temporal lobectomy involving the removal of the hippocampus may in some persons, or under some conditions, have the same effect.

Further evidence of the part played by the temporal lobes in memory has been obtained by electrical stimulation of these structures, using implanted electrodes, inserted for the investigation of temporal lobe epilepsy. Bickford and others (1958), using this method, investigated the effects upon memory of unilateral stimulation. This caused transient confusion with subsequent loss of memory for events following the stimulation and a R.A. the length of which was related to the duration of stimulation. Thus stimulation for 5 seconds caused R.A. for 1 day, stimulation for 10 seconds R.A. for several days, older memories being perfectly recalled (Bickford, 1964). The R.A. was transient, the time taken for recovery being proportionate to the length of R.A. Thus, after stimulation for 5 seconds, recovery took 5 to 10 minutes, after stimulation for 10 seconds it took 1 to 2 hours. If we assume that the effect of stimulation was transient paralysis of temporal lobe structures concerned with memory, these experimental observations fall into line with the effects of temporal lobectomy. They are also of importance as showing a relationship between the duration of inactivation and the length of R.A.
I shall next consider cases of the amnesic syndrome in which, though there is evidence of organic cerebral disorder, its localization is uncertain. Memory disorder following a particular variety of encephalitis as described by Rose and myself (1960) is comparatively rare, but of interest because, though it resembles Korsakoff's psychosis, there are small but significant differences. There is the same combination, as in Korsakoff's psychosis, of a dense, prolonged and persistent R.A. with severe impairment of recent memory, but insight is usually well preserved, and, apart from the defect of memory, intellectual function is practically normal. There is no defect of perception, and though the patient may remember hardly anything of his current experience, he is seldom out of touch with his environment. It seems likely that the encephalitis in these cases was of the same kind as that described by Brierley and others (1960) in post-mortem studies with a noticeable concentration of the lesions in the limbic areas of the brain. Drachman and Adams (1962) have reported similar pathological data, with evidence pointing to the virus of herpes simplex as the cause. The four cases reported by Rose and myself all survived the illness, so that there was no proof of either the localization of the lesion or its pathology. An air encephalogram carried out in one of our patients showed dilated lateral ventricles with well-marked focal dilatation of the anterior temporal horns. It seems probable that in all these four survivors, the main incidence of damage was on the temporal lobes.

The patient in our series (Case 1) who was left with the least disability I have recently examined again, 19 years after the onset of his illness in March 1947, which left him with severe impairment of recent memory and an R.A. which was complete for two years. Events before this time he appeared to recall accurately. He had been in the Merchant Navy before the War, and at its outbreak joined the R.N.R., served mainly in the Far East, rose to the rank of Lieutenant-Commander and was awarded the M.B.E. He recalled the last ship he had served in and a few isolated incidents soon after this. He had, in fact, during the two years after returning to civilian life had a quite eventful existence. He was admitted to the National Hospital in June 1948, where the gross defect of recent memory was confirmed. He had good insight, himself complaining "Things that are going on don't impress themselves on me. It's the immediate things that go." His R.A. showed no improvement under barbiturate hypnosis. Apart from these abnormalities, there was no significant intellectual loss. He retained 8 digits, was reasonably quick and accurate with arithmetical problems, and had an I.Q. of 113 on the Wechsler-Bellevue Test. I saw him later in 1949 and 1958, when there did not seem to be any change in his condition.

The occasion for his seeking my advice this year was doubt expressed by others of his competence to manage his own affairs. He was himself
confident of his own abilities. He had for some time been earning small sums as the local correspondent of several newspapers, and he had recently married a woman of his own age, who at a separate interview with me told me that his memory was impeccable.

He could, as before, retain 8 digits, but his attempts at retaining a name, address and flower, after an interval occupied with other mental activity, failed completely whether the interval was 5, 4, 3 or 2 minutes. His performance was no better after the items were immediately repeated either by himself or the examiner. In two tests carried out without distraction in the intervals, so that he was able to rehearse his answers, he made one error at the 5 minute, and one at the 3 minute interval. With arithmetical problems he was slow and inaccurate. His grasp of current affairs was grossly defective. In answer to question, he told me that the present Prime Minister was Mr. Attlee (which would have been correct at the time of onset of his R.A.). He met my observations on this and similar errors with evasive rationalizations, saying, for example, that he was not interested in the news apart from space travel. His reasoning and judgment tested by discussion of his financial position and future plans were defective. He showed no insight. There was thus evidence of considerable deterioration, which I suspect to be the effect of ageing—he is now 50.

The memory disorder in tuberculous meningitis is of interest because, though at first severe, it clears up entirely in many cases. Williams and Smith (1954) reported their observations in 19 patients. There was amnesia for the period of confusion, often of several weeks, and after this, for a time, defect of recent memory, and a R.A. of variable extent. But when followed up for periods of up to 4 years, though 4 of the patients complained of forgetfulness, there was apparently no psychometric evidence in any of them of impairment of recent memory. Six, however, showed a persistent, though patchy, R.A., which in 4 extended for more than a year, and in one case for 4 years. One of these cases previously reported (Cairns and Taylor, 1949) is a typical example. The onset of the illness was in January 1947. By August of that year tests for recent memory showed no impairment, but he had a R.A. of 4 months for events before the onset of his illness, as well as amnesia for the six months following its onset. The R.A. remained virtually unchanged 3 years later. During the forgotten period he had learned to type, and preserved this skill, though he had no memory of having acquired it (Smith, 1966). These observations are of importance as illustrating the fact that a long and persistent R.A. is not necessarily associated with residual defect of recent memory.

The effects of electro-convulsive treatment (E.C.T.) upon memory have been studied by several observers. They closely resemble the effects
of head injury. After a single shock there is a period of confusion, with subsequent P.T.A. and R.A. The latter may at first be prolonged, but shrinks to a duration of between a few seconds and one minute. After a series of bi-weekly treatments the clinical picture is like that of a more severe head injury. Some years ago there was, for a short time, a vogue for intensive E.C.T., that is, a series of some 30 shocks at the rate of 2 or 3 a day. Stengel (1951) recorded his observations on 10 patients treated by this method, though not by him. All had prolonged clouding of consciousness with amnesia for the period of treatment and thereafter for some days. All had a R.A., at first prolonged, but gradually shrinking. In none, however, was the permanent R.A. less than two days. Even a year after treatment recall for events which had occurred several months before the treatment was patchy. In 4 of his cases the persistent R.A. was much longer, up to several years. As these patients were hysterical subjects, Stengel suspected that the long R.A. might be partly psycho-neurotic. It is to be noted that in these patients there was virtually no evidence of persistent recent memory defect.

It is not stated whether in these cases muscle relaxants were used for the treatments. If, as seems probable, they were not (Stengel, 1966), the memory disorder may have been caused by anoxic damage to the temporal lobes. This, however, cannot be the explanation of the amnesia observed after E.C.T. as now administered. We have to ask ourselves whether the memory disorder here is due to a diffuse cerebral effect of the shock, or whether the hippocampus is selectively involved because of its low epileptic threshold (Liberson et al., 1953).

The case of Mabille and Pitres (1913) has been disregarded because the lesions were remote from the regions ordinarily involved in the amnesic syndrome. There were small areas of old infarction symmetrically placed in the white matter in front of each caudate nucleus. It must at once be admitted that the authors might have failed to observe lesions of the mammillary bodies, but Pitres was an experienced neuroanatomist. The patient, who was not alcoholic, was admitted to hospital for a "stroke" at the age of 34. He had a transient left hemiparesis. He was later transferred to a mental hospital, where the authors examined him some years later. He died of intercurrent disease at the age of 57. The clinical history is inadequate in one respect. There is no estimate of the R.A. That there was a R.A. we can be certain from the evidence, and it was probably for 4 years. His memory for events before that time was accurate. He was able to describe the public buildings, streets and monuments in the town in which he had been brought up, and in Paris, where he had worked some time before his illness. His descriptions were checked by the authors. He had, however, no memory of the sea-port where he was working at the onset of his illness, nor did he recognize the surroundings when taken
there. He showed a gross defect of recent memory, being unable to retain any new information for longer than 15 seconds. Immediate retention was good. Knowledge and skills acquired before the R.A. were preserved. He knew how to play cards. He played draughts and occasionally won.

The authors’ interpretation was that the lesions interrupted the long association bundles between the uncinate, frontal and occipital cortex, and ends with the following conclusion. “Every act of complete memory will involve the successive participation of several centres which are fundamentally distinct. The anatomical substratum of memory will not be represented by a single organ, but by a complex apparatus, of which each portion will be charged with the accomplishment of one of the phenomena which we are accustomed to designate en bloc under the name of memory.” They were of opinion that the temporal lobes were of especial importance in this organization. They regarded the symptoms in their case as those of what would now be called a disconnexion syndrome. They were possibly right.

Head Injuries

Of the clinical material available for the study of memory disorder, the effects of head injuries provide by far the largest quantity. The traumatic amnesias have been fully described by many observers, in particular by Russell (Russell and Nathan, 1946; Russell, 1959), and I shall not go over this ground again. I would only remind you of the main facts concerning retrograde amnesia (R.A.) and post-traumatic amnesia (P.T.A.). There is almost always, even in the slightest case of concussion, an R.A., if only for a few seconds before the injury. In cases of severe injury the R.A. may be at first much longer than this—up to a year or more. It then shrinks during the period of confusion, and thereafter, until it is usually quite brief. The shrinkage proceeds from more remote to more recent time. The P.T.A. on the other hand, remains constant. Thus there is opportunity for correlation of the duration of R.A. and P.T.A., and this has been established in large numbers of cases. The correlation on the whole is close: the longer the P.T.A. the more likely it is that R.A. also will be long. Russell and Nathan (1946) found a permanent R.A. of over 12 hours in 18 out of 200 patients, and, of these 18, 14 had a P.T.A. of over 7 days. The permanent R.A. may sometimes have a duration of months. It is often assumed that an exceptionally long R.A. must be hysterical or malingered. Such a possibility should, of course, always be considered, but the pitfall must be avoided of supposing a symptom to be hysterical because it is unusual. As an example of a long R.A. that I believe to have been the effect of organic brain damage I will present some details of a case I have previously mentioned (Symonds 1962).
The case to be related is that of a housewife, aged 46 when seen in August 1959 by Dr. Hierons two weeks after a closed head injury. She was drowsy and confused, with a moderately severe right hemiparesis and bilateral extensor plantar responses. The confusion cleared in about five weeks, and the right hemiparesis gradually improved, though both plantar responses remained extensor for five months. She was left with a P.T.A. of five weeks. When I examined her with Dr. Hierons a year after the injury she was able to lead a virtually normal life, looking after her home and family without any special disability, though she complained of forgetfulness. There was a very slight weakness of the right limbs, with no other abnormal signs. She appeared to have a moderate defect of recent memory, and had a R.A. of at least one year. She was examined by Professor Zangwill eighteen months after the injury, who confirmed an R.A. of one year with a diffuse and patchy amnesia extending over a further period of 4 or 5 years. She did not, for example, remember the death of her mother-in-law 4 years before the accident. Memory for events of her youth and early married life appeared to be intact. On simple learning tests she reacted like a patient with moderate organic memory defect. Subsequently, at Professor Zangwill’s suggestion, she was investigated under barbiturate hypnosis, with no recovery of R.A.

There are two aspects of this case which invite attention. From the physical signs observed, it appears likely that the patient sustained diffuse brain damage of a long lasting kind. The second point of interest is the discrepancy between only a moderate defect of recent memory and a R.A. of one year.

One of the remarkable features of the R.A. is its limitation in time. The length of the R.A. is commonly judged by the patient’s “last memory” before the injury. Zangwill (1961), in a careful study, has shown that this is not as reliable an end point as clinicians have assumed. During the shrinkage of a traumatic R.A., although the general trend is towards recovery of remote before recent memories, islands of memory are often recalled irrespective of their time sequence, and the gaps subsequently filled in. He has further observed that following severe head injuries after full shrinkage of the R.A., there may be a patchy amnesia for remote events which extends far beyond the ordinarily accepted boundary of the R.A. From my own observations, I believe that the boundary between hazy or scattered memories and total amnesia provides a useful measure for the length of the permanent R.A. For the latter period there is loss of memory for important as well as trivial events, and recognition is usually lost as well as recall. A case reported by Russell and Nathan (1946) provides an example. This patient was an experienced R.A.F. pilot left with a R.A. of a week during which time he had been trained in flying exercises of a new kind. These were recorded in his log-book,
which he had many times studied in a fruitless attempt to recall the memories of these days.

How long can a traumatic R.A. be? I have a note of a youth seen at the age of eighteen who had sustained a head injury at the age of eight with a P.T.A. of several weeks. No sign of focal injury had been apparent. He returned to school and had done well at both work and games. It was only when I made the routine enquiry that I found he had a complete R.A. for the whole of his life before the accident, except for a single incident which he was told had occurred when he was four or five. He was looking out of a window one afternoon during a rainstorm and saw a man crawling along a roof with a ladder. "When," he said, "I try to think of my previous life, that is all that will come." This memory he distinguished absolutely from a past life history he had built up for himself from what he had been told by others. This distinction is often vouchsafed by patients with a long R.A., though others will state that they are uncertain of it.

It is to be observed that in cases of slight concussion there may be P.T.A. without any appreciable clouding of consciousness. The typical instance is that of the football player who, after a minor head injury with such brief loss of consciousness that the game is stopped only for a minute or two, resumes his part in the game without any significant impairment of skill, yet later has no memory of this period, which may be half an hour or more. After more severe injuries, following a period of confusion, a patient may be correctly orientated for time, place and person, and behave and converse normally for several days, yet later have no recollection of this period. For example, an officer admitted to the Oxford Hospital for Head Injuries in a state of drowsy confusion after a closed head injury gradually improved up to a point at which his behaviour was normal, and there was no clouding of consciousness. It was necessary to transfer him to a neighbouring hospital for a minor orthopaedic operation. This I explained to him, and he appreciated all I had to tell him. Ten days later he returned to the Head Injuries Hospital as arranged, but he had no recollection of ever having been there before. Nor did he recognize me or any of the staff or patients with whom he had been previously familiar.

Concerning the localization and pathogenesis of the cerebral damage causing memory disorder in cases of closed head injury we are ignorant, for these patients recover. The clinical picture is on the whole so constant from one case to another that it is reasonable to suppose diffuse rather than focal damage. It has been plausibly suggested (Dixon, 1962) that there is widespread disturbance of the macro-molecular patterns in the neurones. In support of this is the experimental observation in concussed
guinea-pigs of fragmentation and agglutination of the Nissl substance, in which RNA is contained (Windle, Groat and Fox, 1944). An alternative hypothesis proposed by Strich (1961) is that widespread damage to the nerve fibres throughout the cerebral hemispheres may be responsible. She has demonstrated in the brains of patients who have died in a state of semi-coma some months after a closed head injury extensive destruction of nerve fibres, which appears to be the result of rupture at the moment of injury, and suggests that if nerve fibres are stretched rather than torn, the lesions may be reversible at some stage, and may play a part in the production of the signs of concussion. A third possibility is that of selective damage, of a reversible kind, to the temporal lobe. The temporal poles are very often found to be contused in fatal cases of closed injury. But, as has already been remarked, the uniformity of the clinical symptoms in concussion suggests an effect of widespread commotion rather than focal damage.

**Transient Global Amnesia**

Fisher and Adams (1964) have described under the title of Transient Global Amnesia episodes of memory disorder of an unusual kind. I have seen several such cases, and have nothing to add to their full clinical description. The onset is sudden, without any premonitory symptoms, and usually without apparent precipitating cause, though in 2 of their 17 cases the episode was preceded by bathing in cold sea water, and in another 2 cases the onset was during coitus.

There is usually in the initial phase some clouding of consciousness with confusion of mild degree, insight being preserved. The characteristic feature of these episodes is amnesia, both post-ictal and retrograde. The episode lasts for several hours, ending in complete recovery. Following this the R.A. is at first extensive, and may cover a period of days or weeks, but rapidly shrinks. The patient is then left with a permanent R.A., the duration of which is generally proportionate to the P.T.A. (I use P.T.A. here and elsewhere for convenience, although there is no trauma).

The clinical picture closely resembles that observed after concussion. In both conditions the patient may after the onset be capable of behaviour that appears normal, for example, driving through traffic to a correct destination, during a period for which he has no memory. In 16 out of the 17 cases reported by Fisher and Adams there was only a single episode, many of their patients having been followed up for several years. Examination of the data reveals that, as in concussion, the longer the duration of the P.T.A., the longer was the permanent R.A. The average duration of R.A. was, however, longer than that generally observed in concussion. The authors conclude that the clinical symptoms reflect a localized
disorder of function involving the rhinencephalic-diencephalic system specifically concerned with memory. They discuss the possibility of a transient ischaemic basis for the attacks or alternatively a focal epileptic seizure, and tentatively favour the latter. To their illuminating commentary upon the nature of the memory disorder I will refer later.

Meanwhile I would remark upon some of their data which seem to me to support an ischaemic, rather than an epileptic interpretation. There is first the isolated occurrence of the episodes, which is unlike the story of epilepsy. Further, the mean age of their patients was over 62. In 7 of them there was evidence either before, at the time of, or after the attack, indicating or suggesting cerebrovascular disease. In a further case there was severe arterial hypertension, and in another atrial fibrillation. Against the ischaemic hypothesis is the analysis by Fisher of prodromal manifestations in some 200 cases of cerebral thrombosis, with no record of any episode of the kind under discussion. But cases of cerebral thrombosis are common, and transient global amnesia is of rare occurrence. If transient ischaemia is the cause, it would seem that it must be of a focal distribution in those parts of the temporal lobes supplied by the posterior cerebral arteries. We have already noted the occurrence of permanent memory disorder following bilateral infarction of these structures. We cannot invoke a generalized cerebral ischaemia as the cause of these episodes. Nothing of the kind is to be observed, for example, in Stokes-Adams attacks.

Observations on Animals

The operation of memory in subhuman species has been an object of attention for at least a century, witness the classic observations of the behaviour of hunting wasps by Bates (1864) and Belt (1873). Recent studies of these insects have confirmed and extended their observations (Thorpe, 1956), and the behaviour of other species, for example the honey-bee, and birds (Thorpe, 1956) provides further evidence of the same kind.

The training of mammals to learn tasks such as maze learning, and the effects upon learned habits of removal of various parts of the brain, which began with the work of Lashley (1950) on rats, has been extended in recent years to more sophisticated studies in the monkey. Lashley concluded that in rats the loss of learned habits was related not to the site of the experimental lesion but its extent, that is that if a large enough mass of cortex were removed, wherever it might be, the learning would be lost. It has now been shown that this generalization does not apply to monkeys. A monkey can readily be trained to choose between two receptacles according to which was filled with food within the animal's sight a few
seconds previously. After appropriately placed bilateral frontal lobe lesions, the monkey repeatedly fails in this task (Harlow and Settlage, 1948). Bilateral temporal lobe lesions do not produce this effect, but are followed by the loss of learned habits based upon the visual discrimination of patterns (Mishkin and Pribram, 1954; Chow, 1954). This loss, however, does not occur if the habit is “overlearned” before the temporal lobe ablations. This means that after the learning was shown to be successful to the criterion demanded (e.g. 90 per cent success in 30 trials) the animal was given several hundred additional trials (Orbach and Fantz, 1958).

It has further been shown (Chow and Survis, 1958) that in a monkey which, as the effect of overlearning, has retained the visual discrimination habit after bilateral temporal lobe ablation, the habit may be lost after subsequent bilateral ablation of frontal or parietal cortex. Such frontal and parietal lesions are not followed by loss of retention of visual discriminations learned to criterion with intact temporal lobes. Piercy (1964) comments on this that it suggests that overlearning of a single habit provides protection against focal cerebral injury by increasing cerebral equipotentiality for the habit. The principle involved is important. It indicates the possibility that memories of overlearned habits might in time obtain a wide distribution in the cerebral cortex. It has been argued that loss of the learned habits under discussion is due not to defective memory, but to defective perception. This problem in animals is difficult to resolve, but the possibility that we are dealing with experimental memory disorder cannot be ignored.

The work of J. Z. Young (1965) and his colleagues on the octopus is well known and of great potential importance. It has been demonstrated that the octopus can learn to discriminate, either by vision or touch, between objects followed by reward of food and objects followed by trauma in the form of an electric shock. It can thus be trained either to attack or retreat in response to the appropriate visual or tactile stimulus. After ablation of specific parts of its brain the animal’s capacity to learn or retain the habit is impaired or lost. There are separate areas concerned with learning by touch and vision. From the histological study of these areas of brain Young has evolved a concept in neurophysiological terms of memory units or mnemons.

The basic concept in Young’s model is that the signal resulting from the association of a particular environmental stimulus with taste or pain is conveyed to a motor cell possessing two outgoing axons destined respectively to be effective either for attack or retreat. The system is originally biased in favour of attack. A signal of the result of the animal’s response being received at the appropriate site excites an inhibitory interneurone which closes one or other of the outgoing pathways. This
inhibitory block is indefinitely prolonged. The mnemon, in his phrase, is switched. Therefore, if ever the same environmental stimulus is experienced again, only one of the alternative outgoing pathways is available, either that for attack or that for retreat. The advantage of this model is that it provides an interpretation in physiological terms of what happens at a single learning trial. There is, however, no simple mechanism proposed for forgetting, which in man appears to be an active and important function. It may be, however, that in the life of the octopus there is no need for forgetting.

One of the many experiments on the octopus shows the effect of time on forgetting. Each octopus was shown a crab (food) but given a shock if he attacked it. A group of normal animals thus shocked every eight minutes learned not to attack after four trials. A group of animals with ablation of the vertical lobes shocked every eight minutes showed almost no signs of learning after fourteen trials. But when such animals were shocked at four minute intervals they learned not to attack after six trials. Thus, in these animals the capacity for learning was not lost, but the lesson was rapidly forgotten. This I have selected, admittedly out of its context, as what seems to be an instance of accelerated forgetting produced by an experimental lesion.

Psychological Interpretation

The psychological interpretation of the amnesic syndromes has been fully discussed recently by Talland (1965), who proposes as a unitary hypothesis for their solution a defect of retrieval. He postulates a general mechanism for searching and scanning, whether of old memories or new. The defect of memory, whether recent or remote, is due to premature closure of activation of this process. Search and scan cease before there is an adequate match. For this hypothesis he leans a good deal upon the apathy and loss of initiative observed in the 20 patients he has studied over a number of years. These, however, were all except one suffering from a true Korsakoff's psychosis of alcoholic origin. In other cases of the amnesic syndrome there may be no apathy or lack of initiative. Such patients may be observed to strive hard and persistently in the effort to overcome their defects. We cannot, therefore, accept loss of drive as an explanation of faulty search. That a searching and scanning system must operate in recall is evident. It is a process that is probably always active, whether we are awake or dreaming, being largely involuntary and outside consciousness. There are, however, obstacles to Talland's view that a general defect of this operation is the cause of the memory defect. Let us take for instance a patient, who, after a head injury, has a P.T.A. of two weeks, and a R.A. of two days, but with no residual defect of recent memory. Such cases are not uncommon. Recall for events before the
R.A. and after the P.T.A. is unimpaired. There cannot be a general defect of the mechanism for retrieval. The examples given of prolonged R.A. without any corresponding defect of recent memory after tuberculous meningitis and intensive E.C.T. provide further evidence of the same kind.

Talland, in developing his hypothesis, has used the analogy of filing systems. All memories, he supposes, are recorded on many files, in multiple contexts of past experience, affect, interest, intent to remember, and time. Pursuing this analogy, it seems possible that the filing of memories under different contexts is a process that is continuous in time for weeks, months, and years. The more often an item is rehearsed or revived, with changing contexts, the greater the number of files in which it is entered, and consequently the greater number of clues to its recovery. In the filing system as thus imagined the time context, it may be supposed, is of outstanding importance. A serial order of reminiscence provides landmarks for scanning. Loss of anchorage in time appears from clinical observation to be a constant feature of the patchy R.A. that precedes that which is complete. If the consolidation of long term memory storage extends thus far in time, the recall of the more recent memories would be more likely to fail than those more remote. Yet this does not explain the time limitation of the long R.A. It seems that it is not the number of contexts in which a memory has been filed that determines whether it is lost or retained, but rather the length of time for which it has been stored.

Ritchie Russell (1959) has suggested that memories are perpetually reinforced during resting activity of the neurones by the passage of impulses along the already established pathways. The well-worn pathway is better able to survive injury or decay. The objection to this hypothesis is that in normal persons a high proportion of memories are in fact lost with the passage of time. Gooddy (1964) has proposed the analogy of damage to a tape-recorder, in the attempt to solve the problem of R.A. The result of this might be to erase that part of the magnetic pattern which has just emerged from the recording region. It would be swept clear, with a limitation only of time. It appears doubtful, however, whether such a mechanism could explain a R.A., for example, of a year.

Fisher and Adams (1964), in reviewing their data, stress the fact that during the amnesic episode items presented to the patient were correctly perceived, but could not be committed to memory, and this, as we have observed, is a constant feature of the P.T.A. in all the amnesic syndromes. Together with this, they note that items learned immediately before the attack were forgotten, and those experienced days or weeks before could not be remembered until the attack had terminated. They pose the question whether it is a general principle that impaired capacity to lay
down durable memory records is always combined with R.A. and vice versa, and conclude that the answer appears to be in the affirmative, leading to the hypothesis that the same neural apparatus is used in laying down memory records and in recalling experience normally memorized in the past. They consider the possibility that the hippocampal system is as fundamental to the integrated activity of the cortex as is the so-called reticular formation and diffuse projection system of the upper brain stem.

At this juncture it must be remarked that the question asked by Fisher and Adams is not so simple as they perhaps assume. It does appear to be true that during an acute amnesic episode, whether traumatic or of other causation, there is a constant association of R.A. and defect of recent memory. In some instances, for example Korsakoff's psychosis, the post-encephalitic and vascular lesions, and after bilateral temporal lobectomy, this association persists, but in many other instances the capacity to lay down durable memory records is restored, while a R.A. persists.

Neuropsychology of the Amnesic Syndrome

Turning back now to the anatomical and physiological aspects of memory disorder, it appears that memory, both recent and remote, must be largely dependent on the functions of the temporal lobes, mammillary bodies, and parts of the thalamus. The anatomical connexions between these structures lead naturally to the supposition that they constitute a unitary system, which Fisher and Adams (1964) have designated the rhinencephalic-diencephalic system. I shall call it, for convenience, the hippocampal system. It does not follow that the units of the memory organization are stored in this system, which may operate in a facilitating or alerting capacity upon memory units situated elsewhere.

What is remarkable in the amnesic syndromes that we have considered is the uniformity of clinical pattern. There is first loss or disturbance of consciousness, followed by confusion, and after this a defect of recent memory. There is a P.T.A. covering the whole of this period, and there is a R.A. which, if at first extensive, shrinks. After the episode, if there is full recovery, the patient is left with R.A. and P.T.A. without any other defect. If recovery is incomplete, there is also a persistent defect of recent memory. The P.T.A. includes loss of memory for the period of confusion, during which it can be attributed to defective perception. But for the remainder of the P.T.A., when there is no clouding of consciousness, and for the persistent defects of recent memory in cases with incomplete recovery, some other interpretation is required. Looking at this part of our problem from the psychological aspect, we may ask whether the memory defect may not be described in terms of excess, or acceleration, of a natural process of forgetting.
It is clear that under normal conditions forgetting is an immediate and important sequel of perception. As Bartlett (1932) has observed, "Only in relatively few cases and those mostly the product of an elaborately guarded civilization could the retention unchanged of the effects of experience be anything but a hindrance." We observe in our patients that immediate memory, as tested for example by digit span, or name, address and flower retention, is unimpaired, but in the extreme case nothing is remembered for longer than a minute or two. When the disability is less severe, it still appears to be an acceleration of forgetting, so that, for example, the patient remembers at the end of two hours as much as the normal person remembers at the end of twenty-four hours. In this case, what the patient does remember is largely determined by all the factors, such as attitude and interests, which contribute to remembering in the normal person.

The problem of the R.A., and especially the permanent R.A., remains. There is obliteration of memories that must have been normally registered and stored. The loss includes all memories within a certain period of time. The length of time is so variable, and in many instances so long, that the interpretation offered by some authorities of disruption of so-called short term traces before there has been structural modification cannot be accepted. In an attempt to translate clinical observation and psychological analysis into physiological terms, I am going to begin with the assumption that the neural substrate of memory is based upon structural modifications —memory units. These memory units are not the exclusive property of neurones specially adapted for this function, but are conceived as imprints of experience that may be registered in vast numbers of neurones which have other functions. Thorpe (1956), putting this in another way, concludes that any neurones which retain any kind of special memory trace of an experience must certainly also participate in countless other activities. Whether the structural modifications concerned are at synaptic junctions or in the alignment of macromolecules is in the present context of relatively little importance. What is important, however, is the assumption that they are not fixed and irreversible, but subject to change. Such change may be determined by a great many variable factors. Bartlett (1932) long ago, from the psychological aspect, stressed the active components of remembering, dependent upon current attitudes, interests and affect. The factor, however, which is of particular interest in the present discussion is that of the passage of time.

I shall assume that in the structure of the memory units there is an inherent bias towards decay, that is towards forgetting. This bias is strongest in the most recently established memory units, or putting it in another way, the longer the structural modification has existed, the more resistant it is to decay. Decay is imagined to be not an all-or-nothing step,
but a fading of the imprinted pattern that constitutes the identity of the memory unit, fading that will under certain conditions proceed in time to erasure.

The bias towards decay, or forgetting, is normally opposed by what I shall call an activating system, situated mainly in the hippocampal system. These structures are assumed to be connected with the memory units by specific pathways. If the operation of the activating system ceases, decay will prevail. There will be no lasting memories formed during the period of inactivation. This is the P.T.A. It is to be noted that during the later stages of a long P.T.A. the patient may appear to be fully conscious and responding normally to his environment. It is only memory that is non-existent.

During the period of inactivation there will be decay of memories already stored before the brain damage. This decay, for the reason already mentioned, will first affect the most recently established memories, which will quite rapidly decay to zero. The rate and extent of further retrograde loss will depend upon the age of the memory and the duration of inactivation. The longer a memory has been established, the longer it will survive inactivation. The process of decay, however rapid, is gradual. Therefore, beyond the range of time within which all memories have decayed to zero, there will be, at any one time, a zone in which the memory units have decayed to a non-functional level but can gradually recover their function if activation is restored. The shrinkage of R.A. is thus allowed for. I shall suppose also that, although the backward limit of the ultimate R.A. is time determined, other factors may operate to some extent in the process of recovery from partial decay. Hence the existence of isolated memories beyond the R.A. proper.

If there has been permanent damage to the hippocampal system, as after temporal lobectomy or encephalitis, two kinds of memory disorder will be observed (1) accelerated decay, or forgetting, of current memories, (2) a dense R.A. whose forward boundary will be the onset of the P.T.A., and whose backward boundary will be a line drawn in time between memories that have decayed to zero, and those that have suffered from decay, without total extinction. Beyond this line there will be a zone of patchy R.A. with a less-well-defined backward time limit. If, on the other hand, there is complete restoration of the activating system, as in most cases of head injury, memory for current events will return to normal. The R.A., however, having shrunk as far as possible, will persist, owing to the fact that during a period of inactivation, the memories most recently stored will have decayed to zero. The longer the period of inactivation, the longer will be the R.A. Hence the general correlation between duration of P.T.A. and R.A. According to this hypothesis, inactivation and
consequent memory disorder need not necessarily be due to damage of the hippocampal structures. Interruption of the pathways connecting these structures with the memory units might have the same effect. Such damage could possibly account for the amnesia in cases of head injury, and in particular for a persistent long R.A. with little or no defect of recent memory. Under such conditions, in which memories already stored have been deprived of activation for a long time, forgetting will have advanced far in the retrograde direction. But in so far as the activating system itself remains intact the capacity for forming new memories will recover if its connexions with the memory units are restored.

These ideas, it will be noted, have no foundations of physiological fact. Their only justification is that they offer a speculative interpretation of the clinical data in terms of a unitary hypothesis—that of unbalanced forgetting. The hypothesis is not inconsistent with the observation that all memories fade with the passage of time. Decay is progressive despite the opposing force of the activating system, though the memories last to become extinct are commonly the oldest. The organization envisaged would be most conveniently thought of in terms of the representation of memories by macro-molecular patterns in the neurones, at least in its final stage.

Over and over again in our consideration of memory disorder the importance of time has become apparent. It has been aptly said that "Memory is a process whereby organized time-space events are carried forward in time" (Halstead, 1960). For this process the operation of biological clocks must be essential. About these we have learned a great deal in recent years. The existence of Circadian oscillations has been established in almost every form of life that has been adequately examined (Pittendrigh, 1965). These clocks, with their nearly 24-hour periodicity, operate with amazing precision, and are entrained by light to fit the 24-hour cycle. In vertebrates it seems almost certain that the driving centre for Circadian oscillation is in the hypothalamus. There is also evidence for the existence in rat and man of biological clocks with longer periodicities (Richter, 1965). But how these clocks contribute to the physical organization of memory we do not know. We shall better understand disorders of memory when we know more about the physiology of time.

REFERENCES


