WHAT TO DO

Pract Neurol 2009; 9: 85–89

When a patient with epilepsy complains about poor memory

Adam Zeman

Patients with epilepsy often complain of "poor memory". The first step in managing this complaint is a clinical evaluation to define and, if possible, quantify the problem. The memory difficulty may be entirely unconnected to the epilepsy. But if the two appear to be linked, establish whether the memory problem is due to the seizures themselves, the pathology that underlies the seizures, their treatment, or their psychological sequelae such as anxiety or depression. Further management depends on the cause, while practical advice on the amelioration of poor memory can be useful.

Memory complaints are common among people with epilepsy,[1] and were identified as one of the foremost factors impairing quality of life in one large survey.[2] Here I will describe an approach to assessing and managing such complaints. The main steps are:

- Tease out what is meant by "poor memory", and quantify this, if possible, using simple clinical cognitive tests.

A Zeman
Professor of Cognitive and Behavioural Neurology, Peninsula Medical School, Barrack Road, Exeter EX2 5DW, UK;
adam.zeman@pms.ac.uk

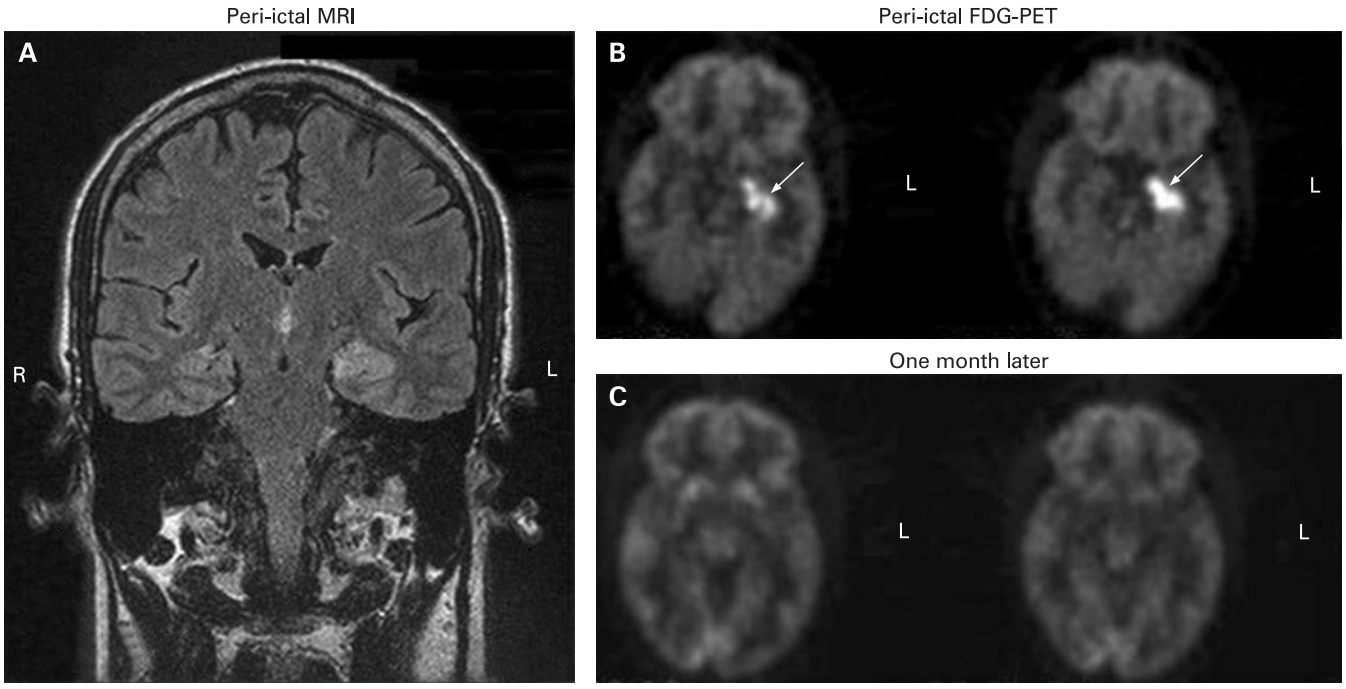

Figure
There is no doubt that certain types of epilepsy can cause memory problems, for example during attacks of transient epileptic amnesia. (A) Coronal fluid-attenuated inversion-recovery MR brain scan shows left (on right of scan) hippocampal oedema at the time of a flurry of attacks, with hippocampal hypermetabolism (demonstrated by PET, (B), arrows) that resolved with treatment of the epilepsy (C).

- Consider the possibility that the memory complaint is unrelated to the epilepsy, requiring an entirely fresh assessment.
- If the memory problem does appear to be bound up with the epilepsy, establish whether it is due to:
  - poor seizure control
  - the underlying pathological process
  - the drugs prescribed
  - the patient's emotional reaction to the predicament caused by the illness.
- Finally, some practical advice can be helpful in ameliorating memory problems.

ASSESSING THE MEMORY COMPLAINT

Complaints of "poor memory" are common but vague, and should be clarified during the history taking. The principle problem may be with:

- *Registration*: if information is not registered it cannot be remembered. A child with frequent absence seizures may be unable to remember what she "learns" at school because the information is not perceived in the first place. Does the history raise the possibility of recurrent brief loss of awareness?
- *Attention*: the clue to an underlying impairment of attention often comes from the report of frequent absent-minded mistakes, like forgetting why one has entered a room. Impairment of attention is common in mood disorder, but can also be caused by drugs and frequent seizures.
- *Anterograde memory*: anterograde amnesia is suggested by difficulty in learning new information even under optimal conditions. "Accelerated long-term forgetting" has recently been identified as a problem for some people with temporal lobe epilepsy,[3] who are able to retain information for hours or days but find that it leaks away unusually rapidly over days to weeks.
- *Retrograde memory*: difficulty in recalling salient past personal events indicates a retrograde amnesia for episodic memories, while difficulty in remembering well-established facts, like the name of the capital of France, indicates a retrograde amnesia for semantic information.

Careful questioning should clarify which of these types of memory problem is the main concern.

Comprehensive history taking is also important in other ways. It will provide much of the background information—about such things as seizure frequency—required to answer the questions discussed later on. Asking some general questions about appetite, sleep, energy levels, the ability to concentrate and mood will help to identify psychological causes for memory disturbance.

10.1136/jnnp.2009.172205

The history also provides an opportunity to decide whether complaints of memory difficulty are likely to reflect real impairment; patients who complain bitterly of memory problems yet can give extremely detailed histories may well be worrying unnecessarily.

Simple approaches to cognitive examination can roughly quantify at least some memory complaints. I use the Addenbrooke's Cognitive Examination-Revised (ACE-R) for clinical assessment.[4] This contains questions sensitive to impairments of attention, anterograde verbal and semantic memory. But tests like this are never comprehensive—for example, they will fail to detect early decline in intelligent people, are insensitive to impairment of visual memory, do not sample memory over long delays, and contain no autobiographical questions. Formal neuropsychological assessment can fill some of these gaps, but not all genuine problems are easily measured. Cognitive testing therefore supplements but cannot replace a good history.

MIGHT THE MEMORY PROBLEM BE COMPLETELY UNRELATED TO THE EPILEPSY?

If clinical assessment suggests the presence of a significant memory disorder in someone with epilepsy, it may of course be unrelated to the epilepsy. This is likely to be true, for example, in someone with well-controlled, long-standing epilepsy who develops memory problems in later life, in whom standard investigations for possible dementia would be appropriate. In general, it is important to be alert to the possibility of additional diagnoses in people with epilepsy.

IF THE PROBLEM IS RELATED TO THE EPILEPSY, HOW IS IT RELATED?

Is it due to the seizures?

Memory involves a series of processes, each of which is probably susceptible to disruption by epileptiform activity: (i) acquisition, (ii) consolidation (the modification of memories over time that accounts for the relative vulnerability of recently acquired memories to various insults to the brain), (iii) storage and (iv) retrieval. Clinical experience, and limited evidence,[5] suggest that frequent seizures can disrupt memory through a combination of ictal and post-ictal effects on these processes. Thus, in any patient with frequent seizures whose memory is poor, treating the seizures—with drugs or surgery—may improve memory function.

Whether subclinical epileptiform activity—apparent on the EEG but without clear-cut seizure manifestations—can disrupt memory is a moot point and requires further research.[6] The rhythmic electrical activity associated with memory processing shares common features with the rhythmic activity that occurs in epilepsy,[7] and it is plausible but unproven that some of the memory impairment occurring in epilepsy may be due to functional disruption by interictal discharges.

In most patients with poor memory due to frequent seizures the problem will be readily apparent, but EEG studies are occasionally required to reveal an unexpectedly high frequency of seizures meriting intensified antiepileptic treatment. Of course, in some cases of medial temporal lobe epilepsy sustained epileptiform discharges may go undetected by scalp EEG.

Is it an independent effect of the pathology causing the seizures?

The process that gives rise to the seizures may, independently (or additionally), give rise to memory impairment, especially if the process involves the medial temporal lobes which play such a key role in memory processing. The pathology in question may be a "structural" lesion, such as a temporal lobe glioma or mesial temporal sclerosis, or a more diffuse process, such as Alzheimer's disease.

In cases of marked acute or subacute memory impairment occurring in patients with epilepsy, the underlying cause of the "epileptic encephalopathy" should be pursued energetically. Possibilities include:

- inherited metabolic disorders, especially, for example, in younger patients with "progressive myoclonic epilepsy"
- cerebral vasculitis
- infections (eg, CJD, herpes simplex, HIV)
- auto-immune disorders (eg, limbic encephalitis associated with antibodies to voltage-gated potassium channels)
- paraneoplastic limbic encephalitis

- acquired metabolic disorders (for example electrolyte disturbance)
- drugs, including alcohol, or drug withdrawal
- degenerative dementias in later life.

Many of these disorders are more likely to cause a confusional state, with pronounced impairment of attention, than a genuinely selective disorder of memory, but this can occur—for example, in limbic encephalitis. Thus where subacute memory loss is associated with unexplained epilepsy, brain imaging, appropriate blood tests, cerebrospinal fluid examination and occasionally other tissue biopsies are indicated.

Is it due to the treatment?

Some patients say that their memory improves when their epilepsy is treated. However, memory can be impaired by therapy and sometimes improved by drug reduction or withdrawal.[8] This is particularly likely in patients with refractory epilepsy taking several agents. Drug effects on memory can be specific or a reflection of more global cognitive impairment. They can be dose-related and predictable, or idiosyncratic:

- Phenobarbitone is now seldom used in the UK as a first line drug but it is still taken by many patients with long-standing seizures; it can cause cognitive impairment, particularly if given in unnecessarily high doses.
- Sodium valproate occasionally gives rise to an extrapyramidal syndrome associated with cognitive slowing.
- Group studies suggest broadly similar risks of cognitive adverse-effects from carbamazepine, sodium valproate and phenytoin.
- The newer drugs, especially lamotrigine, gabapentin and leveteracitam, may be somewhat less prone to, but not free of, such effects.
- Topiramate, a potent antiepileptic, is the exception to this rule; it has pronounced dose-related cognitive adverse-effects in some patients.
- Tiagabine occasionally provokes non-convulsive status epilepticus which can present with "poor memory" due to a confusional state.

Where there is a clear relationship between cognitive impairment and introduction or augmentation of a drug, the possibility of switching to an alternative should be considered and discussed with the patient. A choice must often be made between reducing adverse-effects, by reducing or withdrawing an effective drug, and reducing seizure frequency at the cost of adverse-effects. Decisions about the optimal trade-off between efficacy and adverse-effects require an open conversation.

Is it due to anxiety and depression caused by the epilepsy?

The frequency of mood disorder is increased in patients with epilepsy, and mood disorder impairs memory. Depression is the most frequently identified treatable cause of memory impairment in the clinic. It is therefore important to be on the lookout for mood disorder in patients with epilepsy who have memory complaints. Relevant screening questions for depression include:

- "Have you felt low most of the time over the past two weeks?"
- "Have you been unable to enjoy things over the last two weeks?"

Patients who answer "yes" to both questions are likely to be depressed. There may be associated complaints of poor appetite, disturbed sleep, poor concentration, low energy levels, low self-esteem, and feelings of guilt. Screening questions for anxiety and panic, respectively, include:

- "Do you feel on edge, apprehensive or nervous much of the time?"
- "Do you sometimes feel frightened, get a lot of physical symptoms all at once, like a pounding heart and clammy palms, and want to get away?"

Patients with epilepsy who have depression may benefit from antidepressant treatment. There is thought to be some risk of lowering seizure threshold with antidepressants, and this should be mentioned. However the risk appears to be small with selective serotonin reuptake inhibitors, and modest with tricyclic antidepressants. The possibility of drug interactions—for example, an increase in carbamazepine levels during treatment with

10.1136/jnnp.2009.172205

fluoxetine—needs to be considered. Occasionally depression will benefit from a change of antiepileptic drug, for example from treatment with phenobarbitone. Anxiety may benefit from treatment of depression. Psychological treatment should be considered for both.

PRACTICAL STEPS TO AMELIORATE MEMORY PROBLEMS

These are largely common sense but nevertheless worth mentioning:

Information is more likely to be remembered if it is:

- studied slowly, carefully and repeatedly
- linked to other well-established information to create mnemonics.

Routines and organisation help to minimise memory load in everyday life.

Simple memory aids can be very useful:

- post-it notes
- a notebook or diary
- a white board.

More sophisticated memory aids are available:

- a mobile phone or a personal digital assistant to provide reminders about pills, tasks and appointments.

Several booklets are available giving simple explanations of how memory works and fuller explanations of the techniques for improving memory mentioned above.[9]

PRACTICE POINTS

- Establish exactly what the patient means by "poor memory", an ambiguous complaint.
- If there is a memory deficit, try to quantify it.
- Consider the possibility that its cause is unrelated to the epilepsy.
- If it is related to the epilepsy, establish whether it is due to frequent seizures, their underlying cause, medication or to psychological factors.
- Once the cause is determined, appropriate management can follow. Simple practical advice on improving memory can be helpful.

ACKNOWLEDGEMENTS

I thank Chris Butler, Narinder Kapur, Mike Sharpe and Margaret Jackson, who reviewed this paper, for their helpful comments.

REFERENCES

1. Thompson P, Corcoran R. Everyday memory failures in people with epilepsy. *Epilepsia* 1992;**33**:S18–S20.
2. Fisher RS, Vickrey BG, Gibson P, *et al.* The impact of epilepsy from the patient's perspective I. Descriptions and subjective perceptions. *Epilepsy Res* 2000;**41**:39–51.
3. Butler CR, Graham KS, Hodges JR, *et al.* The syndrome of transient epileptic amnesia. *Ann Neurol* 2007;**61**:587–98.
4. Hodges JR. *Cognitive assessment for clinicians.* Oxford: Oxford University Press, 2007.
5. Jokeit H, Daamen M, Zang H, *et al.* Seizures accelerate forgetting in patients with left-sided temporal lobe epilepsy. *Neurology* 2001;**57**:125–6.
6. Binnie CD. Cognitive impairment during epileptiform discharges: is it ever justifiable to treat the EEG? *Lancet Neurol* 2003;**2**:725–30.
7. Meador KJ. The basic science of memory as it applies to epilepsy. *Epilepsia* 2007;**48**(Suppl 9):23–5.
8. Loring DW, Marino S, Meador KJ. Neuropsychological and behavioral effects of antiepilepsy drugs. *Neuropsychol Rev* 2007;**17**:413–25.
9. Kapur N. *Managing your memory.* Wessex Neurological Centre, 2001.