



## Treatment of dementia

R Overshott and A Burns

*J. Neurol. Neurosurg. Psychiatry* 2005;76;53-59  
doi:10.1136/jnp.2005.082537

---

Updated information and services can be found at:  
[http://jnp.bmj.com/cgi/content/full/76/suppl\\_5/v53](http://jnp.bmj.com/cgi/content/full/76/suppl_5/v53)

---

*These include:*

### References

This article cites 14 articles, 7 of which can be accessed free at:  
[http://jnp.bmj.com/cgi/content/full/76/suppl\\_5/v53#BIBL](http://jnp.bmj.com/cgi/content/full/76/suppl_5/v53#BIBL)

### Rapid responses

You can respond to this article at:  
[http://jnp.bmj.com/cgi/eletter-submit/76/suppl\\_5/v53](http://jnp.bmj.com/cgi/eletter-submit/76/suppl_5/v53)

### Email alerting service

Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article

---

### Topic collections

Articles on similar topics can be found in the following collections

[Neurology in Practice](#) (150 articles)  
[Drugs: central nervous system \(not psychiatric\)](#) (271 articles)  
[Dementia](#) (524 articles)

---

### Notes

---

To order reprints of this article go to:  
<http://www.bmjournals.com/cgi/reprintform>

To subscribe to *Journal of Neurology, Neurosurgery, and Psychiatry* go to:  
<http://www.bmjournals.com/subscriptions/>

# TREATMENT OF DEMENTIA

R Overshott, A Burns

v53

*J Neurol Neurosurg Psychiatry* 2005;76(Suppl V):v53–v59. doi: 10.1136/jnnp.2005.082537

**D**ementia describes a chronic and progressive clinical syndrome characterised by cognitive impairment (particularly memory loss), inability to perform activities of daily living, and neuropsychiatric features (psychiatric symptoms and behavioural disturbances, also known as behavioural and psychological symptoms of dementia or BPSD). It affects an estimated 800 000 people in the UK and four million in the USA. Alzheimer's disease (AD) is the most common cause of dementia (60%), followed by vascular dementia (VaD) (20%) (although 20% of people have both AD and VaD) and dementia with Lewy bodies (DLB) (15%). There have been significant advances in treatments available for dementia in the last few years.

## ▶ CHOLINESTERASE INHIBITORS

Cholinesterase inhibitors (ChEIs) are the mainstay of treatment of Alzheimer's disease. Randomised controlled trials (RCTs) have reported statistically significant, and clinically modest, effects of ChEIs. Trials have been short, conducted over six months, although effects have been reported, in open label extensions, to last up to five years. The primary aim of the trials has been to assess the treatment response for cognitive decline. This is most often measured using the Alzheimer's disease assessment scale (ADAS-Cog),<sup>1</sup> which assesses multiple cognitive outcomes and is an accepted standard for measuring cognitive abilities in clinical trials. The total score of the ADAS-Cog ranges from 0–70, the higher score indicating greater impairment. Over a six month period untreated patients with mild to moderate AD typically deteriorate as signified by an increase of 3–4 points on the ADAS-Cog. Patients with moderate to severe AD have an increase of 4–6 points over the same period of time.<sup>2</sup> The Cochrane Review of donepezil for AD found an improvement at 24 weeks of 2.9 on the ADAS-Cog compared with placebo.<sup>3</sup> Similar findings were reported in the Cochrane reviews of galantamine<sup>4</sup> and rivastigmine.<sup>5</sup> Another primary aim of trials has been to assess changes in subjects' functional abilities. This is measured using a global assessment such as the clinician's interview-based impression of change plus caregiver input (CIBIC-plus).<sup>6</sup> A subjective interview by a clinician with a patient and caregiver, assessing the patient's function, in four areas determines whether overall the patient has improved, stayed the same or deteriorated, using a 7 point scale. If an effect is detected during the clinician's interview it is assumed that it is clinically relevant. The Cochrane Reviews<sup>3–5</sup> dichotomised rating scale data into those who had no change or improvement versus those who worsened and found a statistically significant effect in favour of treatment, with an odds ratio of approximately 2. The Cochrane Reviews also report significant improvements on rating scales for activities of daily living and neuropsychiatric symptoms. The Cochrane Review of donepezil for AD<sup>3</sup> reports a low dropout rate of under 20%, with similar numbers for treatment and control groups within a study, except for the treatment group taking 10 mg/day of donepezil which had slightly higher dropout rates.

Apart from Cochrane Reviews there have been several other meta-analyses that conclude there is a significant benefit from treatment with ChEIs. There are, however, concerns regarding the quality of evidence and the size of the benefits, which are felt, by some, to be minimal.<sup>7</sup> It has been suggested that many systematic reviews have not stringently assessed the quality of studies<sup>7</sup> and that most, if not all, ChEIs trials have flawed methodology, which questions their validity. There is also a shortage of evidence of improvement of quality of life using validated, dementia specific measures, while pharmacoeconomic evaluations of ChEIs have so far been conducted in retrospect.

## NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE GUIDANCE

Although they are not a cure, ChEIs currently offer the best hope in treating AD. Initially the availability in the UK of ChEIs for the treatment of AD depended on where patients lived rather than their clinical need, so called "post code prescribing". The National Institute for Health and Clinical Excellence (NICE) 2001 guidelines for the treatment of AD with ChEIs<sup>8</sup> recommended their use.

See end of article for authors' affiliations

Correspondence to:  
Dr Ross Overshott, Department  
of Old Age Psychiatry, 2nd  
Floor, Education and Research  
Centre, Wythenshawe  
Hospital, Manchester, M23  
9LT, UK; [rovershott@fs1.with.man.ac.uk](mailto:rovershott@fs1.with.man.ac.uk)

The future use of ChEIs in the UK for National Health Service (NHS) patients is, however, again in doubt following the publication of NICE's new draft guidance.<sup>9</sup> They have maintained their position from 2001 that the medications have an effect and are safe in the treatment of AD, but have now concluded that the drugs are not cost effective and should not be reimbursed by the NHS. NICE received over 4000 responses, their largest ever, during the initial consultation period of the new guidelines. NICE reported that since the publication of its original guidelines the clinical evidence base for ChEIs has matured and that it demonstrates a consistent gain on cognitive and global scales compared to placebo in mild to moderate AD.<sup>9</sup> They were concerned that the effects are small and there is little positive randomised evidence available on the long term gain of ChEIs. Despite these concerns, NICE concluded that ChEIs were effective but were not cost effective and therefore would no longer be recommended. It has been felt by many that NICE's appraisal had several shortcomings which influenced their conclusions regarding cost effectiveness. They had underestimated the cost of full-time institutional care and had not fully considered the full benefits for carers. It has been estimated that ChEI treatment costs £2.50 a day and yet there is evidence to suggest that treatment can reduce carer input by half an hour a day.<sup>10</sup> For a professional carer this would constitute a saving of at least £2.50 a day: the price of ChEI for one day.

The economic model used by NICE also did not reflect the use of ChEIs in clinical practice, where treatment is discontinued in patients who do not respond. The NICE model, however, assumes that all patients continue with treatment irrespective of response. Their analysis, therefore, included patients who had not responded and were not gaining any benefit from treatment but were still accumulating costs. In clinical practice these patients' treatment would be discontinued and the cost curtailed.

Patients, carers, clinicians, and interested organisations have been confused by the change of stance by NICE in their new draft guidelines, as the evidence for the effectiveness of ChEIs has improved since their original guidelines, which recommended the treatments. At the time of writing, NICE have postponed their final assessment and are considering further information.

### DONEPEZIL, GALANTAMINE, AND RIVASTIGMINE

There are currently three ChEIs regularly used in the UK that are licensed for the treatment of mild to moderate AD: donepezil, galantamine, and rivastigmine. They have each been shown to produce the benefits of ChEI treatment mentioned earlier and in practice there is very little to choose between them in terms of core efficacy. Donepezil (Aricept) comes in two doses (5 and 10 mg) and until recently had the unique advantage of once a day prescribing. The dose for rivastigmine (Exelon) ranges from 1.5–12 mg a day and has a butyrylcholinesterase action in addition to acetylcholinesterase. Galantamine (Reminyl) has a nicotinic receptor allosteric action and has just become available in an extended release daily capsule.

### INITIATING TREATMENT WITH CHOLINESTERASE INHIBITORS

Once a diagnosis of AD has been made it is important to discuss in detail with the patient and their relative/carer what treatment will entail. For most the diagnosis of a dementia

**Table 1** NICE guidance for the treatment of Alzheimer's disease

- ▶ Alzheimer's disease must be diagnosed in a specialist clinic where assessments should include cognitive and behavioural functioning, activities of daily living, and likelihood of compliance with treatment
- ▶ Treatment should be initiated by specialists but may be continued by general practitioners
- ▶ The carer's views should be sought before and during treatment
- ▶ Treatment should only be commenced in patients with mild or moderate Alzheimer's disease whose MMSE score is above 12 points
- ▶ The patient should be assessed 2–4 months after a maintenance dose is established. Treatment should only continue if the MMSE has improved or not changed and if behavioural or functional assessment shows improvement
- ▶ The patient should be assessed every 6 months. Treatment should usually only continue if MMSE score remains above 12 and it is considered that treatment is having a worthwhile effect on functioning and behaviour

MMSE, mini mental state examination.

can be devastating and understandably they may have high expectations, sometimes unrealistic, of any treatments offered. It is therefore important to be clear from the outset on several key points:

- ▶ The medications are not a cure.
- ▶ The medications do not work for everyone. The rule of thirds in medicine applies approximately: one third get better, one third do not deteriorate further, and in one third it makes no difference and the patient deteriorates at the rate as if untreated.
- ▶ The medication will be discontinued if the patient does not respond to it.

The NICE guidance<sup>8</sup> (table 1) published in 2001 provided a structure which includes systematic monitoring which, although under review, provides a sensible template for the prescription of the drugs.

It has been suggested that the primary aim of the guidelines is to contain prescribing and control drug costs.<sup>11</sup> The guidance certainly lacks some practical elements. It is, for example, important for patients to have an electrocardiogram (ECG) before starting a cholinesterase inhibitor, as bundle branch block is a relative contraindication to their prescription. A set of practical guidelines for initiating treatment with cholinesterase inhibitors is set out in table 2.

### WHICH CHOLINESTERASE INHIBITOR SHOULD BE STARTED AND BY WHOM?

There is no real difference in the effectiveness of the three cholinesterase inhibitors. The few comparative studies published are small and have been conducted over a relatively short period. The results are inconsistent and offer no basis to make a clinical choice.

Rivastigmine has the reputation of more commonly causing side effects, particularly nausea and vomiting. This may be due to the initial dosing regimen being too quick (table 3); slowing the titration period to four instead of two weeks will help reduce the side effects. To reduce nausea rivastigmine should be taken with food. As both galantamine and rivastigmine have additional modes of action, apart from acetylcholinesterase (AChE) inhibition, many clinicians believe they are more effective in later stages of AD when AChE concentrations are low.

The current NICE guidelines stipulate that prescribing should be initiated by specialists but may be continued by general practitioners under a shared-care protocol. This

**Table 2** Initiating treatment with cholinesterase inhibitors

- ▶ Establish diagnosis of Alzheimer's disease using standardised criteria (for example, ICD-10) through interviewing the patient, taking a collateral history, and undertaking a cognitive assessment. The patient should have a full dementia blood screen and neuroimaging, when appropriate, to identify co-morbidities and reversible causes of cognitive impairment
- ▶ Explain and discuss diagnosis, prognosis, and treatment options with patient and carer
- ▶ Agree a treatment plan with involvement from a multidisciplinary team. Suggest and encourage the patient and carer to contact the local branch of the Alzheimer's Society
- ▶ Establish baseline scores for cognitive function, global functioning, neuropsychiatric symptoms, and activities of daily living using standardised rating scales
- ▶ Commence cholinesterase inhibitor
- ▶ Make sure an ECG has been conducted recently to exclude problems with cardiac conduction
- ▶ Monitor the patient's progress regularly using clinical skills and standardised rating scales

ECG, electrocardiogram; ICD-10, International classification of diseases, 10th revision.

means that after an initial phase the patient receives their ChEI from the same source as their other medication which reduces confusion and improves the likelihood of compliance.

### SIDE EFFECTS OF CHOLINESTERASE INHIBITORS

The three ChEIs have broadly similar side effect which are summarised in table 4. The most common side effects are gastrointestinal and are usually transient, lasting a few weeks. Most patients are able to continue on the medications while side effects pass. Gastrointestinal effects can be limited by slow titration and taking the medication with food. If nausea and vomiting are problematic, treatment with an anti-emetic should be considered. Rivastigmine may be particularly prone to causing gastrointestinal side effects as it is the ChEI which inhibits butyrylcholinesterase (BuChE) which is found in the gastrointestinal tract.

The inhibition of AChE may increase parasympathetic tone, therefore ChEIs should be used with great caution in

**Table 3** Dosing requirements for cholinesterase inhibitors

- ▶ Donepezil
  - start on 5 mg once a day
  - if tolerated, increase to 10 mg once a day
  - maximum dose: 10 mg a day
- ▶ Galantamine
  - start on 4 mg twice a day and after 4 weeks increase to 8 mg twice a day
  - according to response and tolerance, increase to 12 mg twice a day
  - maximum dose: 12 mg twice a day
- ▶ Rivastigmine
  - start on 1.5 mg twice a day and after 2 weeks, increase to 3 mg twice a day
  - after at least another 2 weeks consider increasing dose to 4.5 mg twice a day
  - according to response and tolerance the dose can be increased to 6 mg twice a day
  - maximum dose: 6 mg twice a day

**Table 4** Main side effects of cholinesterase inhibitors

- ▶ Nausea
- ▶ Vomiting
- ▶ Diarrhoea
- ▶ Anorexia
- ▶ Abdominal pain
- ▶ Headache
- ▶ Dizziness
- ▶ Tremor
- ▶ Weight loss
- ▶ Fatigue

patients with bradycardia, sick sinus syndrome, or cardiac conduction disturbances.

### SWITCHING CHOLINESTERASE INHIBITORS

There have been few published studies on switching ChEIs, although it has been reported that over 50% of patients will gain benefit from the new ChEI.<sup>12</sup> Current opinion is that medications can be changed overnight.

### STOPPING CHOLINESTERASE INHIBITORS

When a patient who has only recently started treatment does not appear to be responding to a ChEI there are three options:

- ▶ increase the dose
- ▶ switch to another ChEI
- ▶ withdraw the drug and consider memantine.

A more difficult decision is when to stop a ChEI in a patient who has responded but there is a suspicion, based on either a global impression or deterioration on a rating scale, that the treatment effect is wearing off. The NICE guidelines<sup>8</sup> recommend discontinuation once the mini mental state examination (MMSE) score is below 12, but as ChEIs can provide other benefits it is perhaps wise to consider the possibility of effectiveness in all areas, not just cognition, before discontinuing treatment.

The risks and benefits of stopping must be discussed fully with the patient and carer. If there is doubt about whether a drug is doing more harm than good a trial of withdrawal is appropriate. Clinicians often find that stopping a ChEI in a patient leads to an unexpected deterioration of behaviour (for example, increased agitation) or cognition, proving the drug was having more of an effect than realised. When attempting withdrawal it is important to monitor closely for any deterioration in order that the medication can be reinstated quickly so the same level of symptomatic effect can be regained.

### USE OF CHOLINESTERASE INHIBITORS IN OTHER DEMENTIAS

Cholinergic deficits are also found in patients with VaD and DLB. There is growing support for the use and effectiveness of ChEIs in these dementias and so far no indication that their use should be managed differently from ChEI treatment for AD.

### Dementia with Lewy bodies

ChEIs are being increasingly used as the first line pharmacological treatment for DLB. They have been shown to provide symptomatic improvement of apathy, delusions, and hallucinations.<sup>13</sup> The cholinergic deficit in DLB is thought to

be greater than in AD and it has been hypothesised that patients with DLB have a better response to ChEI than those with AD. As patients with DLB often tolerate antipsychotic medications poorly, ChEIs provide the most practical option for treating the neuropsychiatric symptoms found in DLB. ChEIs are not licensed for use in DLB but are being increasingly used

### Vascular dementia

There is a treatment effect of ChEIs in patients with AD and cerebrovascular disease and there is growing evidence of similar benefits in VaD only. Cholinergic structures are vulnerable to ischaemic changes which can lead to significant loss of cholinergic neural pathways although rarely to the magnitude seen in AD. Donepezil and galantamine have been shown to have a significant effect on cognition and global function, and estimated effect sizes are similar to those seen in the first trials for AD.<sup>14</sup> ChEIs, however, are still not licensed, and therefore rarely used, for the treatment of VaD. With recent doubts over the future of ChEI use in AD, this is unlikely to change in the near future.

### Parkinson's disease with dementia

Rivastigmine has been shown in one trial to produce significant improvements in cognition, global ratings of dementia, and behavioural symptoms which were of the same magnitude observed in ChEI trials for AD.<sup>15</sup> ChEIs are frequently, despite not being licensed, prescribed for the treatment of neuropsychiatric symptoms of Parkinson's disease with dementia. ChEIs have not been found to worsen the motor symptoms of Parkinson's disease.

### MEMANTINE

Memantine, a partial glutamate receptor antagonist, is the only drug licensed in the UK for the treatment of moderate to severe AD. It has, however, been used in Germany for over 20 years for various neurological symptoms and cognitive impairment. It was not included in NICE's 2001 guidelines<sup>8</sup> and therefore does not require the same monitoring as ChEIs, although many dementia treatment clinics include patients treated with memantine in their ChEI treatment protocols. The new NICE draft guidelines<sup>9</sup> did, however, include memantine and, as for ChEIs, its use was not recommended because of lack of cost effectiveness.

### Use of memantine in dementia

Despite only being licensed for use in moderate to severe dementia in AD, memantine has been shown to have beneficial effects in slowing deterioration in cognition in patients with mild to moderate AD and VaD too.<sup>16</sup>

The initial dose is 5 mg once a day which should be increased in 5 mg increments at intervals of at least one week until a maximum dose of 10 mg twice a day is reached. Memantine is generally better tolerated than the ChEIs. The most common adverse events of memantine include dizziness, headaches, fatigue, diarrhoea, and gastric pain. In clinical experience the side effects which are most likely to lead to discontinuation are restlessness and hyperexcitation.

Memantine currently is predominantly used in the treatment of moderate to severe AD when it is felt that ChEIs are no longer effective. They also have a role as an alternative to ChEIs in the treatment of patients with mild to moderate AD who are either unable to tolerate ChEIs or when ChEIs are

contraindicated—for example, problems with cardiac conduction.

### COMBINATION THERAPY

A donepezil–memantine combination performed significantly better than donepezil–placebo on cognition, activities of daily living, and behavioural neuropsychiatric scales in a randomised controlled trial. The combination was well tolerated.<sup>17</sup>

### OTHER DRUG TREATMENTS FOR DEMENTIA

ChEIs and memantine are the mainstay of treatment, but other agents have been tried which have generally been unsuccessful.

*Ginkgo biloba*—There have been mixed results in the trials, but meta-analysis shows a small but statistically significant benefit on cognition relative to placebo.<sup>18</sup> The effect is smaller than the effect found with ChEIs.

*Non-steroidal anti-inflammatory drugs (NSAIDs)*—Observational studies have found an association between anti-inflammatory drugs and lower risk of AD, but the result of clinical trials are negative.<sup>19</sup>

*Oestrogens*—Trials have not been successful and several safety problems have arisen, including increasing risk of venous thrombosis.

*Selegiline*—A systematic review of selegiline concluded that although there is some evidence of improvement in cognition and activities of daily living in dementia in the short term, the magnitude was not clinically important.<sup>20</sup>

*Vitamin E*—Vitamin E may maintain the functional status of people with AD.<sup>21</sup> There is no evidence to suggest it can help prevent dementia or improve cognitive function.

### MANAGEMENT OF VASCULAR DEMENTIA

The main focus here is primary and secondary prevention, by controlling risk factors to reduce vascular events. Early identification and treatment of hypertension, which is also a risk factor for AD, with agents such as the angiotensin converting enzyme inhibitor perindopril has been shown to reduce the risk of dementia among patients who have experienced stroke.<sup>14</sup> Lipid lowering medications are also important in secondary prevention of stroke and may protect against dementia. Other factors which are crucial in reducing the risk of vascular dementia are stopping smoking, weight reduction, control of atrial fibrillation with anticoagulation, and nutritional education.

**Table 5** Types of behavioural and psychological symptoms of dementia (BPSD)

- ▶ Aggression
- ▶ Agitation
- ▶ Apathy
- ▶ Biting
- ▶ Delusion
- ▶ Depression
- ▶ Hallucinations
- ▶ Kicking
- ▶ Restlessness
- ▶ Screaming
- ▶ Shaking
- ▶ Poor sleep
- ▶ Wandering

**Table 6** Non-pharmacological approaches for the treatment of BPSD**Verbal therapies**

- ▶ Behavioural therapy
- ▶ Cognitive behavioural therapy
- ▶ Interpersonal therapy
- ▶ Reality orientation
- ▶ Reminiscence therapy
- ▶ Validation therapy

**Non-verbal therapies**

- ▶ Aromatherapy
- ▶ Bright light therapy
- ▶ Exercise and activities
- ▶ Multisensory therapy
- ▶ Music therapy

**TREATMENT OF BEHAVIOURAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA**

Behavioural and psychological symptoms of dementia (BPSD) refer to a group of symptoms and behaviours summarised in table 5.

BPSD are common in all types of dementia, and 80% of patients will experience them during the course of their illness. They are more common in patients with severe dementia and certain types of dementia—for example, DLB, where psychotic symptoms occur in more than 80% of patients. BPSD cause distress for both the patient and carer and are associated with increased carer burden and institutionalisation.

The first line treatment for BPSD has been psychotropic medication, particularly antipsychotic drugs. There has,

however, been growing concern<sup>22</sup> over the use of the medications as they are associated with:

- ▶ increased cognitive decline
- ▶ increased rate of stroke
- ▶ parkinsonism
- ▶ risk of cardiac arrhythmias
- ▶ increased risk of falls
- ▶ increased mortality.

An increasing number of non-pharmacological therapies (table 6) are now available and should be considered before pharmacological treatment.

Table 7 outlines strategies and questions a clinician should contemplate when faced with a patient with BPSD.

An assessment needs to be made of what the current symptoms are. It is imperative that the clinician excludes an underlying medical cause. Agitation, for example, can often occur when a patient has a urinary tract infection or is constipated. The patient may also be in pain and it is reasonable if suspicion is high and the patient, because of their cognitive impairment, is unable to confirm that they are in pain to give a trial of an analgesic to see if the BPSD improves.

A brief outline of approaches to both pharmacological and non-pharmacological treatment will be described for the broad groups of BPSD. For a more in-depth discussion see Overshott *et al.*<sup>23</sup>

**AGITATION****Non-pharmacological interventions Overshott *et al***

Agitation and aggression are probably the BPSD which causes the most distress among patients and their carers. Before a treatment plan can be organised there needs to be some understanding of the behaviours and symptoms. Behavioural management techniques systematically document behaviours,

v57

**Table 7** Management of behavioural and psychological symptoms**1. What are the symptoms?**

- ▶ What behaviours are being exhibited?
- ▶ Is the patient depressed or hallucinating?
- ▶ Is there evidence of apathy or sleep disturbance?

**2. What is the diagnosis?**

- ▶ Does the patient have an established diagnosis of dementia? Which type?
- ▶ Is there an underlying medical condition causing a delirium on top of the dementia?
- ▶ Arrange appropriate physical investigations—for example, infection screen. Is the patient in pain?

**3. Examine the behaviours**

- ▶ ABC (antecedents, behaviours and consequences) analysis of behaviours
- ▶ Is there a pattern?
- ▶ Education for carers (for example, how to approach the patient, sleep hygiene)

**4. Consider non-pharmacological therapies**

- ▶ Is there a role for other therapies?
- ▶ For example, aromatherapy, music therapy for agitation, bright light therapy for sleep disturbance

**5. Consider pharmacological therapies**

- ▶ Review response to interventions so far.
- ▶ If symptoms are still distressing or unmanageable consider starting pharmacological treatment
- ▶ Is the use of a cholinesterase inhibitor indicated?
- ▶ If starting an antipsychotic or benzodiazepine, initiate treatment cautiously with a low dose
- ▶ For example, daily dose, in divided doses:
  - promazine 50–200 mg
  - lorazepam 0.5–2 mg
  - clomethiazole 1–3 caps/5–15 ml syrup
  - trazodone 50–300 mg

using a diary or chart, and record the triggers, behaviours, and reinforcements. This approach is also known as ABC: antecedents, behaviours, and consequences. For example, it may be found that the patient is only agitated when sat in a particular chair because they feel a draft or only becomes restless when a certain visitor leaves. The analysis also provides an opportunity to understand the behaviours from the patient's perspective: what are they trying to tell us?

Reality orientation (RO), reminiscence therapy (RT), and validation therapy (VT) have all been shown to have a positive effect, to some extent, on behaviour, social interaction, and well being, although not cognition. All three therapies can be provided on an individual basis or in groups. The strongest evidence is for the efficacy of RO which is widely used and involves reminding patients with dementia, through discussion and presentation of materials, facts about themselves, current affairs, and their environment. RT uses similar techniques to RO except it focuses on past events and helps the patient relive pleasant earlier experiences, especially significant events such as weddings. VT attempts to communicate with the patients by empathising with the feelings and meanings hidden behind their confused speech and behaviour. In VT there is validation of the patient's current experience. RO and RT are easier therapies to implement on a formal or informal basis and in clinical experience less likely to cause distress than VT.

Several therapies centring on sensory stimulation have been shown to be effective in reducing agitation and behavioural problems. The two main essential oils used in aromatherapy for dementia are lavender and Melissa, which are relaxants and thought to modulate neurotransmitter actions. Aromatherapy can be administered, to suit the patient, via several routes including inhalation, bathing, massage, and topical application. There have so far been few side effects reported. Music therapy delivered via various methods (for example, live/taped music, patient's choice/relaxation music, and listening/playing) has also been reported as an effective treatment,<sup>23</sup> while the findings for bright light therapy (BLT) have so far been mixed. Multi-sensory therapy of Snoezelen, which stimulates the primary senses of sight, hearing, touch, taste, and smell through the use of lighting effects, tactile surfaces, meditative music, and aromatherapy, may also be useful.

### Pharmacological interventions

The evidence for ChEIs, although not unequivocal, is promising with regards to treating agitation. Few studies have rarely had neuropsychiatric symptoms as their primary outcome but, as already discussed, they may be the safest and most effective pharmacological treatment, especially in DLB.

Antipsychotic medications have, without doubt, been overused in the past. Ironically there is no overwhelming evidence to support their use. Of all atypical antipsychotics, risperidone has the largest database of double blind controlled trials to support its efficacy and safety in the treatment of agitation, aggression, and psychosis associated with dementia.<sup>24</sup> Its superiority over placebo for agitation appears to be independent of dementia type, dementia severity, presence of psychosis, or drug induced somnolence. Risperidone, however, along with olanzapine, in the UK is felt to be unsuitable for patients with dementia because of the concerns about increased risk of stroke and mortality.<sup>25</sup> As atypical antipsychotics have a more favourable side effect profile than typical antipsychotics, there is no compelling reason

to recommend the use of more traditional antipsychotics. In fact it has been reported that risperidone and olanzapine are not associated with a statistically significant risk of stroke compared with typical antipsychotics.<sup>26</sup> As with starting any medication, the possible risks and benefits of antipsychotic medication must be considered. With the concerns about atypical antipsychotics, older medications such as promazine and benzodiazepines, which have their own considerable side effects, have come back in vogue. Other alternatives, which have limited evidence available, are carbamazepine, valproate, and trazodone.

### APATHY

Apathy is often ignored and underdiagnosed. It is commonly defined as a lack of interest, emotion, and motivation.

### Non-pharmacological interventions

Caregivers often become frustrated with apathetic patients as they misinterpret their loss of motivation as being disinterested and lazy. Educating caregivers can reduce distress and blame directed towards the patient. Interventions, including behavioural techniques, which optimise functioning, initiate goal directed behaviours, and increase involvement in pleasant activities are also useful.

### Pharmacological interventions

There have been very few studies of any medications, but all three ChEIs have been shown to be effective in the treatment of apathy.

### DEPRESSION

Depression is common in AD, with a prevalence of approximately 20% and even higher in VaD and DLB. It can be very difficult to diagnose depression accurately in dementia. The patient may not be able to report their symptoms reliably due to impaired memory and insight. Observations and collateral history can therefore be important in making the diagnosis. Depression symptoms are often present in patients with dementia in the absence of coexistent depression.

### Non-pharmacological interventions

Cognitive behavioural therapy and interpersonal therapy may have significant benefits in the treatment of depression in dementia,<sup>27, 28</sup> but are likely to be limited in patients with severe dementia. Many other non-pharmacological therapies have been shown to result in improvements, including RO, RT, VT, music therapy, exercise, and recreational activities. Most of these therapies are simple to implement and should probably be the first choice in treating mild-moderate depressive symptoms.

### Pharmacological interventions

Most clinical trials of antidepressants for depression in dementia have been inconclusive. Pharmacological treatments should probably be reserved for patients with severe depression symptoms. The preferred choice of antidepressant is selective serotonin reuptake inhibitors (SSRIs), as tricyclic antidepressants can give cholinergic side effects which increased cognitive and functional impairments in people with dementia.

### PSYCHOSIS

#### Non-pharmacological

There are few non-pharmacological interventions which are useful in treating "true" psychosis. Correcting visual and

hearing impairment and improving lighting can reduce the risk of misinterpretations. Modifying sensory stimulations that may trigger psychosis, such as reflections in a mirror or window, can also be effective.<sup>29</sup>

### Pharmacological interventions

ChEIs, as already discussed, are a safe and effective treatment for psychosis in dementia, particularly DLB. The use of antipsychotics raises the same issues as their role in treating agitation. If a patient is distressed by psychotic symptoms and they have not responded to a ChEI, or a ChEI is not indicated, then the benefits of antipsychotic treatment probably outweigh the risks.

### SUMMARY

Dementia is distressing for patients, their families, and their carers. While a cure for any type of dementia is unlikely in the near future, current symptomatic treatments offer genuine hope for improving the quality of life of patients and carers. All patients should have access to proven safe and effective treatments. Early, accurate diagnosis is essential so ChEIs can be commenced at the earliest opportunity. Management of BPSD should be patient and carer centred, utilising the full range of non-pharmacological treatments available. Prescribing drugs for BPSD should no longer be automatic and instead should be considered carefully.

### Authors' affiliations

**R Overshott, A Burns**, Department of Old Age Psychiatry, Wythenshawe Hospital, Manchester, UK

Competing interests: Dr Overshott has worked on clinical trials sponsored by pharmaceutical companies, including a trial for memantine in Parkinson's disease with dementia. Professor Burns has been involved in clinical trials on cholinesterase inhibitors for Alzheimer's disease which have been sponsored by their manufacturers. He has also received honoraria and hospitality from pharmaceutical companies.

### REFERENCES

- Rosen WG, Mohs RC, Davies KL. A new rating scale for Alzheimer's disease. *Am J Psychiatry* 1984;**141**:1356-64.
- Stern RG, Mohs RC, Davidson M, et al. A longitudinal study of Alzheimer's disease: measurement, rate, and predictors of cognitive deterioration. *Am J Psychiatry* 1994;**151**:390-8.
- Birks JS, Harvey R. Donepezil for dementia due to Alzheimer's disease. *The Cochrane Database of Systematic Reviews* 2003, issue 3.
- Loy C, Schneider L. Galantamine for Alzheimer's disease. *The Cochrane Database of Systematic Reviews* 2003, issue 4.
- Birks J, Grimley Evans J, Iakovidou V, et al. Rivastigmine for Alzheimer's disease. *The Cochrane Database of Systematic Reviews* 2000, issue 4.
- Schneider LS, Olin JT, Doody RS, et al. Validity and reliability of the Alzheimer's disease cooperative study - clinical global impression of change.

- The Alzheimer's disease cooperative study. *Alzheimer Dis Assoc Disord* 1997;**11**(suppl 2):S22-32.
- Kaduszkiewicz H, Zimmerman T, Beck-Bornholdt H-P, et al. Cholinesterase inhibitors for patients with Alzheimer's disease: systematic review of randomised clinical trials. *BMJ* 2005;**331**:321-7.
- National Institute for Health and Clinical Excellence. *Guidance on the use of donepezil, rivastigmine and galantamine for the treatment of Alzheimer's disease*. London: NICE, 2001, <http://www.nice.org.uk/page.aspx?0=14400>.
- National Institute for Health and Clinical Excellence. Appraisal consultation document: donepezil, rivastigmine, galantamine and memantine for the treatment of Alzheimer's disease. London: NICE, 2005, <http://www.nice.org.uk/page.aspx?0=245908>.
- Sano M, Wilcock GK, van Baelen B, et al. The effects of galantamine treatment on caregiver time in Alzheimer's disease. *Int J Geriatr Psychiatry* 2003;**18**:942-50.
- Grimley Evans J, Wilcock G, Birke J. Evidence-based pharmacotherapy of Alzheimer's disease. *Int J Neuropsychopharmacol* 2004;**7**:351-69.
- Auriacombe S, Pere JJ, Loria-Kanza Y, et al. Efficacy and safety of rivastigmine in patients with Alzheimer's disease who to benefit from treatment with donepezil. *Com Med Res Opin* 2002;**18**:129-38.
- McKeith I, Del Sen T, Spano P, et al. Efficacy of rivastigmine in dementia with Lewy bodies: a randomized, double-blind, placebo controlled international study. *Lancet* 2000;**356**:2031-6.
- Erkinjuntti T, Roman G, Gauthier S, et al. Emerging therapies for vascular dementia and vascular cognitive impairment. *Stroke* 2004;**35**:1010-17.
- Emre M, Aarsland D, Albanese A, et al. Rivastigmine for dementia associated with Parkinson's disease. *N Engl J Med* 2004;**351**:2509-18.
- Potyk D. Treatments for Alzheimer disease. *Southern Medical Association* 2005;**98**:628-35.
- Tariot PN, Farlow MR, Grossberg GT, et al. Memantine treatment in patients with moderate to severe Alzheimer's disease already receiving donepezil: a randomized controlled trial. *JAMA* 2004;**291**:317-24.
- Kurz A, Van Baelen B. Ginkgo biloba compared with cholinesterase inhibitors in the treatment of dementia: a review based on meta-analysis by the Cochrane Collaboration. *Dement Geriatr Cogn Disord* 2004;**18**:217-26.
- Tariot PN, Federoff HJ. Current treatment for Alzheimer disease and future prospects. *Alzheimer Dis Assoc Disord* 2003;**17**:5105-13.
- Wilcock G K, Birks J, Whitehead A, et al. The effect of selegiline in the treatment of people with Alzheimer's disease: a meta-analysis of published trials. *Int J Geriatr Psychiatry* 2002;**17**:175-83.
- Sano M, Ernesto C, Thomas RG, et al. A controlled trial of selegiline, alpha-tocopherol or both as a treatment for Alzheimer's disease. The Alzheimer's disease cooperative study. *N Engl J Med* 1997;**336**:1216-22.
- Ballard C, Cream J. Drugs used to reduce behavioural symptoms in people with dementia or an unacceptable chemical cost? Argument. *Int Psychogeriatr* 2004;**17**:4-12.
- Overshott R, Byrne J, Burns A. Non-pharmacological and pharmacological interventions for symptoms in Alzheimer's disease. *Expert Rev Neurotherapeutics* 2004;**4**:809-21.
- De Deyn PP, Katz IR, Brodaty H, et al. Management of agitation, aggression and psychosis associated with dementia: a pooled analysis including three randomized, placebo-controlled double-blind trials in nursing home residents treated with risperidone. *Clin Neural Neurosurg* 2005;**107**:497-508.
- Department of Health. Public Health Link CEM/CMO/2004/1. *Antipsychotics and Stroke*. London: Department of Health, 2004, <http://199.228.212.132/doh/embroadcast.nsf/>.
- Hermann N, MAMDANI KM, Lanctot KL. Atypical antipsychotics and risk of cerebrovascular accidents. *Am J Psychiatrists* 2004;**16**:1113-15.
- Teri L, Logsdon RG, Uomoto J, et al. Behavioural treatment of depression in dementia patients: a controlled clinical trial. *J Gerontol B Psychol Sci Soc Sci* 1997;**52**:159-66.
- James I, Powell I, Kendall K. A cognitive perspective on training in care homes. *Journal of Dementia Care* 2003;**11**:22-4.
- Cohen-Mansfield J. Non-pharmacological interventions for psychotic symptoms in dementia. *J Geriatr Psychiatry Neurol* 2003;**16**:219-24.