Study	Intervention	BPSD	Study design/Follow-up	Outcomes relevant to behaviour	Significance	Quality rating
ChEIs and/or m	nemantine					
Alagiakrishnan et al. 2003 (1)	Rivastigmine 3-6mg/d 2 months	Disinhibition/ sexual aggression	<ul><li>Single case study</li><li>Mixed AD and VaD</li><li>No f/u</li></ul>	Observation by carer report	Sexually aggressive behaviours decreased.	case study
Brodaty et al. 2006 (2)	Galantamine Variable dosage 6 months	Depression BPSD	<ul> <li>Prospective, open-label study</li> <li>345 persons with mild to moderately severe AD</li> <li>No f/u</li> </ul>	CIBIC-plus	Percentage of those who improved was greater than those who worsened on measures of aggression, personality changes, agitation, hallucinations, sleep disturbance, irritability, depression and inertia both at 3 and 6 months.	moderate
Chan et al. 2006 (3)	Rivastigmine 3-12mg/d 20 weeks	Depression BPSD	<ul> <li>Prospective, open-label study</li> <li>24 patients</li> <li>Mild to moderately severe AD</li> <li>No f/u</li> </ul>	Chinese NPI (CNPI)	Significant reductions were observed in CNPI total as well as the delusions, depression/dysphoria, apathy, disinhibition, irritability/lability, aberrant motor behaviour and night-time behaviour disturbance subscales.	moderate
Cummings et al. 2004 (4)	Galantamine 8, 16, 24mg/d 21 weeks	Apathy BPSD	<ul> <li>RCT</li> <li>978 patients</li> <li>Mild to moderate AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI-10 NPI-D	Galantamine associated with improved existing behavioural problems. Less emergence of new behavioural problems, including apathy in the 16mg/day group	strong
Cummings et al. 2006 (5)	Donepezil 5-10mg/d 20 weeks	Aggression Agitation VDB BPSD	<ul> <li>Open-label observational study</li> <li>120 patients</li> <li>AD</li> <li>No f/u</li> </ul>	NPI CMAI BEHAVE-AD	NPI scores improved over the course of 20 weeks of donepezil treatment ( $p < .001$ ). CMAI scores for physically non-aggressive and verbally non-aggressive behaviours, but not physically or verbally aggressive behaviours, also improved ( $p < .001$ and $p < .05$ ). BEHAVE-AD scores were also reduced at	strong
					the end of the intervention ( $p < .005$ and $p < .0001$ ).	

Cummings et al. 2006 (6)	Memantine 20mg/d 24 weeks	Aggression BPSD	<ul> <li>RCT</li> <li>404 patients</li> <li>AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI	Agitation/aggression and irritability reduced in memantine group both at weeks 12 and 24 compared to placebo ( <i>p</i> < .05).	strong
Edwards et al. 2007 (7)	Galantamine 8-24mg/d 24 weeks	Psychotic symptoms BPSD	<ul><li>Open-label study</li><li>50 patients</li><li>DLB</li><li>No f/u</li></ul>	NPI	Total NPI ( <i>p</i> = .01) and hallucinations ( <i>p</i> < .004) subscale scores decreased significantly.  No significant improvements reported on other NPI subscales.	moderate
Erkinjuntti et al. 2002 (8)	Galantamine 24mg/d 6 months	Apathy	<ul> <li>RCT</li> <li>592 patients</li> <li>VaD/AD with cerebrovascular disease</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI	Apathy improved significantly from baseline in galantamine group. No change from baseline in placebo group	strong
Feldman et al. 2001 (9)	Donepezil 5-10mg/d 24 weeks	Apathy	<ul> <li>RCT</li> <li>290 patients</li> <li>Moderate to severe AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI-NH	Significant reduction in apathy reported (p = .0018).	strong
Feldman et al. 2005 (10)	Donepezil 5-10mg/d 24 weeks Post hoc analysis of subgroup of 145 patients from Feldman et al. 2001 (9; see above)	Apathy BPSD	<ul><li>RCT</li><li>145 patients</li><li>Severe AD</li><li>No f/u</li></ul>	NPI-NH	Differences favouring donepezil reported at 24 weeks, including 11/12 NPI measures. Significant reductions reported for donepezil on apathy ( $p = .0116$ ), anxiety ( $p = .0380$ ) and depression ( $p = .0348$ ) subscale scores when compared with placebo.	strong
Fox et al. 2012 (11)	Memantine 20mg/d 12 weeks	Agitation BPSD	<ul> <li>RCT</li> <li>153 patients from carehomes or hospitals</li> <li>AD with clinically significant agitation</li> <li>No f/u</li> </ul>	CMAI NPI	No evidence of difference on CMAI between memantine and placebo. Greater improvement reported on NPI total in the intervention group.	strong
Gauthier et al. 2002a (12)	Donepezil 5-10mg/d 24 weeks Post hoc analysis of subgroup of	Apathy BPSD	<ul> <li>RCT</li> <li>290 patients</li> <li>Moderate to severe AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI-NH	Significant symptom improvement reported for donepezil on apathy ( $p = .0359$ ), anxiety ( $p = .0114$ ) and irritability ( $p = .0086$ ) subscale scores when compared with baseline.	strong

Gauthier et al. 2002b (13)	Donepezil 5-10mg/d 24 weeks Post hoc analysis of subgroup of	Apathy BPSD	<ul> <li>RCT</li> <li>207 patients</li> <li>Moderate AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI-NH	Significant reductions reported for donepezil on apathy ( $p = .0131$ ), delusions ( $p = .0073$ ) and aberrant motor behaviour ( $p = .0232$ ) subscale scores as well as mean change scores for NPI total ( $p = .0022$ ) when compared with placebo.	strong
Gauthier et al. 2007 (14)	Rivastigmine 3-12mg/d 6 months	Apathy BPSD	<ul> <li>Open-label observational study</li> <li>2119 patients</li> <li>Mild to moderate AD</li> <li>No f/u</li> </ul>	Abbreviated CGI-C	Improvements in anxiety (62.3%), apathy (62.6%) and agitation (56%) reported at 6 months.	strong
Gauthier et al. 2010 (15)	Rivastigmine 3-12mg/d 12 months	Agitation ND	<ul> <li>Prospective, open-label observational study</li> <li>3800 patients</li> <li>Mild to moderate AD</li> <li>No f/u</li> </ul>	CGI-C	Percentages of patients experiencing improvements (physician-reported) of each symptom were higher than the percentages of patients experiencing worsening of symptoms at 6 months and 12 months.	moderate
Gauthier et al. 2008 (16)	Memantine 20mg/d 24-28 weeks	Agitation Aggression BPSD	<ul> <li>Pooled analysis of 6 RCTs</li> <li>1826 patients</li> <li>Moderate to severe AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI	Reduced NPI total, agitation/aggression and irritability/lability scores at weeks 12 and 24 or 28 in intervention group when compared to placebo ( <i>p</i> <.05).	strong
Gauthier et al. 2005 (17) Post hoc analysis of data from 2 previous trials: Reisberg et al. 2003 (18) and Tariot et al. 2004 (19)	Reisberg: Memantine 20mg/d 28 weeks  Tariot: Memantine 20mg/d 24 weeks	Apathy	<ul> <li>RCT</li> <li>Reisberg: 252 patients</li> <li>Tariot: 404 patients already taking donepezil for &gt;6 months</li> <li>Moderate to severe AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI	A nonsignificant trend toward improvement in apathy reported on Memantine.	strong

Herrmann et al. 2005 (20)	Galantamine 16, 24, 32mg/d 3-6 months	Apathy BPSD	<ul> <li>Pooled analysis of 3 RCTs</li> <li>2033 patients:         galantamine n = 1347         placebo n = 686</li> <li>Mild to moderate AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI	Significant reduction in total NPI score, agitation/aggression, anxiety, disinhibition and aberrant motor behaviour with galantamine.  Significant changes with galantamine in following clusters:  delusions-hallucinations disinhibition-elation-aberrant motor behaviour hallucinations-anxiety-apathy-aberrant motor behaviour.	strong
Holmes et al. 2004 (21)	Donepezil 5-10mg/d 18 week	Apathy	<ul> <li>RCT with open-label phase</li> <li>96 patients</li> <li>AD &gt; 6 months</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI	Significant improvement in apathy reported at 24 weeks with Donepezil.	strong
Howard et al. 2007 (22)	Donepezil 10mg/d 12 weeks	Agitation BPSD	<ul> <li>RCT</li> <li>259 patients</li> <li>AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	CMAI NPI	No significant differences in CMAI or NPI scores found between donepezil group and placebo group after 12 weeks.	strong
Levin et al. 2009 (23)	Memantine 5-20mg/d 16 weeks	Aggression	<ul> <li>Open-label, controlled study</li> <li>23 patients; memantine n = 14, control n = 9</li> <li>DLB</li> <li>No f/u</li> </ul>	Behavioural Impairments Scale (clinician ratings)	Reduced levels of aggression reported in memantine group when compared with control group at week 16 ( <i>p</i> < .05).	moderate
Litvinenko et al. 2008 (24)	Galantamine 8-16mg/d 24 weeks	ND Psychotic symptoms BPSD	<ul> <li>Open-label, controlled study</li> <li>41 patients</li> <li>Mild to moderate PDD</li> <li>No f/u</li> </ul>	NPI-NH	Significant reductions reported in total NPI scores ( $p = .009$ ), hallucinations ( $p = .0002$ ), anxiety ( $p = .04$ ), apathy ( $p = .006$ ) and sleep disturbances ( $p = .044$ ) for intervention group.	moderate
Mahlberg et al. 2007 (25)	Rivastigmine 3mg/d 2 weeks	Agitation Psychotic symptoms BPSD	<ul> <li>RCT</li> <li>20 patients</li> <li>AD</li> <li>Single-blinded</li> <li>No f/u</li> </ul>	Actigraphy NPI	Agitation significantly reduced ( <i>p</i> = .002) in rivastigmine group when compared to placebo.  Nonsignificant trend toward reduced total NPI scores as well as diurnal and evening activity in the rivastigmine group when compared to placebo.	strong

McKeith et al. 2000a (26)	Rivastigmine 6-12mg/d 20 weeks	Apathy BPSD	<ul> <li>RCT</li> <li>120 patients</li> <li>DLB</li> <li>Double-blinded</li> <li>3-week f/u</li> </ul>	NPI	Initial improvements in apathy, anxiety, delusions, hallucinations and aberrant motor behaviour reported with rivastigmine not significant at 3-week f/u.	strong
McKeith et al. 2000b (27)	Rivastigmine 3-12mg/d 20 weeks blinded 12 weeks open	Apathy BPSD	<ul> <li>RCT with open-label phase</li> <li>11 patients</li> <li>DLB</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI	Mean apathy scores over 12 weeks decreased by 63%. NPI subscale scores for delusions decreased 73%, hallucinations decreased 27%, and agitation decreased 45%.	moderate
Moraes et al. 2006 (28)	<b>Donepezil</b> 5-10mg/d 6 months	ND	<ul> <li>RCT</li> <li>35 patients</li> <li>AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	Polysom- nography	REM sleep significantly increased in the donepezil group while it decreased in the placebo group ( $p < .01$ ). No effects reported for other sleep variables.	strong
Rockwood et al. 2007 (29)	<b>Galantamine</b> 8-24mg/d 4 months	VDB	<ul> <li>RCT with open-label phase</li> <li>37 patients</li> <li>Mild to moderate AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	Goal Attainment Scaling (caregiver rating of verbal repetition)	Significantly more patients in the galantamine group met treatment goal of reduced verbal repetition at the end of the placebo-controlled phase ( $p < .01$ ) but benefits not sustained at conclusion of the open-label phase.	moderate
Swanberg 2007 (30)	Memantine 20mg/d 3 months	Agitation BPSD	<ul><li>Case series</li><li>3 patients</li><li>FTD</li><li>No f/u</li></ul>	NPI	Improvement reported on NPI total score and on agitation, apathy and anxiety subscales.	case series
Tanaka et al. 2008 (31)	<b>Donepezil</b> 3-5mg/d 12 weeks	Aggression Psychotic symptoms BPSD	<ul> <li>Prospective, post-marketing survey</li> <li>252 patients</li> <li>Mild to moderate AD</li> <li>No f/u</li> </ul>	Clinician ratings	Post-intervention, 65.6% of patients reported improvement in aggression while 1.6% reported worsening. 60.1% reported improvement in hallucinations/delusions while 1.3% reported worsening. 59.6% reported improvement in wandering as opposed to 3.4% who reported worsening.	moderate
Tangwongchai et al. 2009 (32)	<b>Galantamine</b> 8-24mg/d	ND Psychotic symptoms BPSD	<ul> <li>Open-label study</li> <li>75 patients</li> <li>AD/VaD/AD with cerebrovascular disease</li> <li>No f/u</li> </ul>	BEHAVE-AD	Significant reduction in paranoid and delusional ideation as well as diurnal rhythm disturbances reported at week 8 maintained throughout intervention period $(p < .05)$ .	moderate

Tariot et al. 2001 (33)	<b>Donepezil</b> 5-10mg/d 24 weeks	Apathy BPSD	<ul> <li>RCT</li> <li>208 patients</li> <li>AD/AD with cerebrovascular disease</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI	No significant differences reported between donepezil and placebo groups in NPI subscores at any assessment point.	strong
Wilcock et al. 2008 (34)	Memantine 20mg/d 24-28 weeks	Aggression Agitation Psychotic symptoms	<ul> <li>Pooled analysis of 3 RCTs</li> <li>983 patients</li> <li>Moderate to severe AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI	Significantly greater proportion of the intervention group experienced reduction in agitation/aggression when compared with placebo at weeks 12 ( $p$ = .011) and 24 or 28 ( $p$ < .001).  Significantly greater reduction in NPI cluster score in intervention group than placebo group for agitation/aggression, delusions and hallucinations at weeks 12 ( $p$ = .0014) and 24 or 28 ( $p$ = .0004).	strong
Typical antipsy	/chotics					•
Burgio et al. 1992 (35)	Haloperiodol vs Oxazepam Variable dosage Variable treatment period	VDB	<ul> <li>Behavioural microanalysis study</li> <li>21 patients</li> <li>AD/multi-infarct dementia/mixed dementia</li> <li>Single-blinded</li> <li>No f/u</li> </ul>	Observation	No observable difference in disruptive vocalisations or paranoid vocalisations (statistics not reported).	moderate
Atypical antips	sychotics					•
De Deyn et al. 2004 (36)	Olanzapine 1.0mg/ 2.5mg/ 5.0mg/ 7.5mg/d 10 weeks	Apathy BPSD	<ul> <li>RCT</li> <li>652 patients: <ul> <li>1.0mg n = 129</li> <li>2.5mg n = 134</li> <li>5.0mg n = 125</li> <li>7.5mg n = 132</li> <li>placebo n = 129</li> </ul> </li> <li>AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI BPRS	Significant improvement in apathy scores reported for those treated with olanzapine 5.0mg only, when compared to baseline scores.  Significant reduction in overall BPSD scores reported in those treated with olanzapine 7.5mg.	strong

Dhikav et al. 2007 (37)	<b>Olanzapine</b> 5mg/d	Disinhibition	<ul> <li>Single case study</li> <li>Moderate AD with delusions, hallucinations and disinhibited sexual behaviour</li> <li>No f/u</li> </ul>	Observation	Sexual disinhibition reportedly reduced.	case study
Goldberg & Goldberg 1997 (38)	Risperidone 0.5-1.0mg/d 6 months	VDB	<ul> <li>Observational study</li> <li>109 patients</li> <li>AD/multi-infarct dementia/mixed dementia/PDD</li> <li>No f/u</li> </ul>	Verbal outbursts questionaire	Reduction in VDB reported. Statistics not reported.	modest
Hamuro & Saito 2010 (39)	Blonanserin Mean dosage of 3.8mg/d at end-point	Aggression Anxiety Apathy Psychotic symptoms BPSD	<ul><li>Case series</li><li>5 patients</li><li>AD</li><li>No f/u</li></ul>	NPI	Three patients reportedly continued to display BPSD at the end of 12 weeks.  Treatment was discontinued in remaining 2 patients due to adverse effects.	case series
Holmes et al. 2007 (40)	Risperidone 0.5-1mg/d Rivastigmine 3-6mg/d 6 weeks	Agitation	<ul> <li>RCT</li> <li>27 patients</li> <li>Severe AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	CMAI	Significantly greater improvements reported in risperidone group on CMAI scores at 6 weeks when compared to rivastigmine group ( $p = .002$ ).	strong
Kopala & Honer 1997 (41)	Risperidone 1-1.5mg/d	VDB	<ul> <li>2 Case studies</li> <li>Moderate to severe dementia/multi-infarct dementia</li> <li>No f/u</li> </ul>	Observation	Reduction in VDB reported. No statistics reported.	case studies
Kurlan et al. 2007 (42)	Quetiapine 25-300mg/d	Agitation Psychotic symptoms BPSD	<ul> <li>RCT</li> <li>40 patients</li> <li>DLB/PDD/AD with Parkinsonian features</li> <li>Double blinded</li> <li>No f/u</li> </ul>	BPRS NPI	No significant differences reported between quetiapine and placebo groups on any measures.	strong
Laks et al. 2006 (43)	Aripiprazole 7.5-15mg/d 14 weeks	Agitation Psychotic symptoms	<ul><li>Single case study</li><li>Severe AD with mild VaD</li><li>No f/u</li></ul>	NPI	Reported reduction in agitation and delusions on15mg dose following dosage increase from 7.5mg. Improvements maintained after dose reduced to 11.75mg due to adverse effects.	case study

Lee et al. 2007 (44)	Clozapine Variable dosage	Agitation	<ul> <li>Systematic chart review</li> <li>16 patients</li> <li>PDD/other dementia</li> <li>Single-blinded</li> <li>No f/u</li> </ul>	BARS CMAI-SF	Reduction in BARS and CMAI-SF scores reported for clozapine.	moderate
Mauri et al. 2006 (45)	Amisulpride 100-200mg/d 12 weeks	Agitation Psychotic symptoms BPSD	<ul><li>Open-label study</li><li>18 patients</li><li>AD</li><li>No f/u</li></ul>	NPI	Reported reduction in NPI total score ( $p < .01$ ) as well as agitation/aggression ( $p < .01$ ), anxiety ( $p < .01$ ), delusions ( $p < .05$ ) and irritability ( $p < .05$ ) NPI subscale scores.	moderate
MacKnight & Rojas- Fernandez 2000 (46)	Quetiapine 25mg/d 2 months	Disinhibition	<ul><li>Single case study</li><li>No f/u</li></ul>	Observation	Disinhibited behaviour ceased within 2 days. Effect maintained at 2 months.	case study
Onor et al. 2006 (47)	Quetiapine 12.5-50mg/d 12 weeks	Aggression ND Psychotic symptoms BPSD	<ul> <li>Repeated measures design</li> <li>41 patients</li> <li>AD/VaD/mixed dementia/DLB/PDD</li> <li>No f/u</li> </ul>	NPI BEHAVE-AD	Significant reduction in levels of delusions, hallucinations, agitation/aggression, depression, anxiety, apathy, irritability, aberrant motor activity, sleep disturbances and carer distress on NPI scores reported at $4 \ (p < .01)$ and $12 \ \text{weeks} \ (p < .05)$ when compared to baseline.  Significant reduction in paranoid and delusional ideation, diurnal rhythm disturbances, affective disturbances and anxiety and phobias on BEHAVE-AD scores at $4 \ (p < .001)$ and $12 \ \text{weeks} \ (p < .05)$ .	moderate
Onor et al. 2007 (48)	Risperidone Mean dosage 1.5mg/d at endpoint 12 weeks	Agitation Aggression Psychotic symptoms BPSD	<ul> <li>Repeated measures design</li> <li>135 patients</li> <li>Mild to moderate AD</li> <li>No f/u</li> </ul>	NPI BEHAVE-AD	Significant reduction in all NPI subscale scores except for appetite disorders as well as caregiver distress at 4 and 12 weeks when compared to baseline ( <i>p</i> < .001).  Significant reduction in all BEHAVE-AD subscale scores at 4 and 12 weeks when compared to baseline ( <i>p</i> < .001).	moderate
Prakash et al. 2009 (49)	Quetiapine 12.5-75mg/d	Disinhibition	<ul> <li>Single case study</li> <li>DLB with inappropriate sexual behaviour</li> <li>No f/u</li> </ul>	Observation	Marked improvements in behaviours reported.	case study

Rabinowitz et al. 2007 (50)	Risperidone 0.25-4mg/d 12 weeks	VDB	<ul> <li>Pooled analysis of 3         placebo-controlled RCTs</li> <li>479 patients:         risperidone n = 313         placebo n = 166</li> <li>Psychosis of AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	CMAI	Reduction in cursing or verbal aggression $(p = .004)$ and repetitive sentences or questions $(p = .025)$ reported but not screaming, constant requests for attention or complaining.	strong
Rappaport et al. 2009 (51)	Aripiprazole 5, 10, 15mg/d 24 hours	Agitation	<ul> <li>RCT</li> <li>129 patients:     aripiprazole 5mg n = 12     aripiprazole 10mg n = 78     aripiprazole 15mg n = 13     placebo n = 26</li> <li>AD/VaD/mixed dementia</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	PANSS-EC ACES	Decreases in PANSS-EC scores were greater in aripiprazole groups compared to placebo throughout 24 hours, with the exception of aripiprazole 5mg dose at 6 and 24 hours.  Reported improvements in ACES scores in aripiprazole groups ≥ those in placebo group, with the exception of aripiprazole 5mg at 1, 1.5, 2, 6 and 24 hours.	moderate
Rocca et al. 2007 (52)	Risperidone / Olanzapine / Quetiapine Variable dosage 6 months	Aggression BPSD	<ul> <li>Retrospective, naturalistic study</li> <li>58 patients</li> <li>AD</li> <li>No f/u</li> </ul>	NPI	No significant difference in drug effects reported but agitation/aggression was significantly reduced at end-point overall when compared to baseline ( <i>p</i> < .001).	moderate
Sato et al. 2006a (53)	Perospirone Variable dosage 6 weeks	Aggression	<ul><li>Case series</li><li>6 patients</li><li>AD/VaD</li><li>No f/u</li></ul>	BEHAVE-AD	Significant reduction in scores on aggressiveness subscale at weeks 2, 4 and 6 when compared to baseline ( <i>p</i> < .01).	moderate
Sato et al. 2006b (54)	Perospirone Variable dosage 6 weeks	Aggression	<ul> <li>Repeated measures design</li> <li>18 patients</li> <li>AD/VaD</li> <li>No f/u</li> </ul>	BEHAVE-AD	Within the aggressiveness factor, significant improvements reported in verbal outbursts and agitation but not physical threats or violence at 6 weeks.	moderate

Savaskan et al. 2006 (55)	Quetiapine 25-200mg/d Haloperidol 0.5-4mg/d 5 weeks	Anxiety ND Psychotic symptoms BPSD	<ul> <li>Randomised, open-label study</li> <li>22 patients</li> <li>AD</li> <li>No f/u</li> </ul>	NPI Actigraphy	Significantly reduced delusions ( $p = .017$ ) and agitation ( $p = .016$ ) reported for both medications. Reduced depression reported for Quetiapine ( $p = .031$ ) and anxiety ( $p = .052$ ). Increased aberrant motor activity ( $p = .035$ ) reported for haloperidol  No significant effects on sleep-wake cycle reported. However, the quetiapine group experienced shorter wake bouts ( $p = .023$ ) while the haloperidol group showed fewer but longer immobile phases during sleep ( $p = .023$ )	moderate
Streim et al. 2008 (56)	Aripiprazole 2-15mg/d 10 weeks	Psychotic symptoms Anxiety	<ul> <li>RCT</li> <li>256 patients</li> <li>AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI-NH BPRS CMAI CSDD	<ul> <li>= .053 and p = .01).</li> <li>Mean changes for aripiprazole on NPI-NH and BPRS psychosis subscales were not significantly different from those of the placebo group.</li> <li>Some improvements were observed, however in anxiety, NPI total, BPRS total CMAI and CSDD.</li> </ul>	strong
Suh et al. 2006 (57)	Risperidone vs Haloperidol 0.5-1.5mg/d 8 weeks each	Agitation ND VDB Wandering BPSD	<ul> <li>Crossover RCT</li> <li>120 patients</li> <li>AD/VaD/mixed dementia</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	BEHAVE-AD (Korean) CMAI (Korean)	Significantly greater reductions reported in wandering ( $p$ = .0496), agitation ( $p$ = .0091), diurnal rhythm disturbances ( $p$ = .0137), anxiety ( $p$ = .0088) for risperidone when compared to haloperidol on BEHAVE-AD.  Significantly greater reductions reported in pacing and aimless wandering ( $p$ = .0123), intentional falling ( $p$ = .0398), hoarding ( $p$ = .0499), performing repetitious mannerisms ( $p$ = .0048), repetitive sentences or questions ( $p$ = .0025), complaining ( $p$ = .0101), negativism ( $p$ = .0027) and physical sexual advances ( $p$ = .0202) for risperidone when compared to haloperidol.	strong

Sultzer et al. 2008 (58)	Olanzapine / Quetiapine / Risperidone Variable dosage 12 weeks	Psychotic symptoms BPSD	<ul> <li>RCT</li> <li>416 patients</li> <li>AD</li> <li>Single-blinded</li> <li>No f/u</li> </ul>	NPI BPRS	Significantly greater improvements reported for risperidone on BPRS psychosis factor when compared to placebo ( <i>p</i> = .010).  No significant differences reported between treatment groups and placebo on BPRS total scores.	strong
Tariot et al. 2006 (59)	Quetiapine 25-600mg/d Haloperidol 0.5-12mg/d 10 weeks	Psychotic symptoms BPSD	<ul> <li>RCT</li> <li>284 patients</li> <li>AD with psychosis</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	BPRS NPI-NH	No significant treatment effects reported for psychotic symptoms.  Improvement reported on BPRS total score for all groups i.e. did not differ from placebo.	strong
Verhey et al. 2006 (60)	Olanzapine 2.5, 5, 7.5mg/d Haloperidol 1, 2, 3mg/d	Agitation Psychotic Symptoms BPSD	<ul> <li>RCT</li> <li>58 patients</li> <li>Dementia</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	CMAI (Dutch) NPI	Significant improvements on NPI hyperactivity factors ( <i>p</i> < .001) but not psychosis factor in both groups.  Both groups reported improvements from baseline on CMAI total and NPI total, but no between-group differences reported.  Improvements in both groups also reported on individual NPI items for delusions, agitation/aggression, anxiety, irritability, aberrant motor behaviour and appetite/eating abnormalities.	strong
Zhong et al. 2007 (61)	Quetiapine 100, 200mg/d 10 weeks	Agitation Psychotic symptoms	<ul> <li>RCT</li> <li>333 patients</li> <li>AD/VaD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	PANSS-EC NPI-NH CMAI	Significantly greater improvements on PANSS-EC reported in the quetiapine 200mg/d group when compared to placebo $(p = .014)$ but not in the quetiapine 100mg/d group $(p = .457)$ .  No between-group differences were observed in NPI-NH or CMAI scores.	strong
Antidepressan	ts					
Banerjee et al. 2011 (62)	Sertraline 50-150mg/d Mirtazapine 15-45mg/d 39 weeks	Depression	<ul> <li>RCT</li> <li>326 patients</li> <li>AD with depression</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	CSDD	Severity of depression decreased in all three groups across time, but the effects of the antidepressants were similar to placebo.	strong

Cakir & Kulaksizoglu 2008 (63)	Mirtazapine 15-30mg/d 12 weeks	Agitation	<ul> <li>Prospective, open-label study</li> <li>16 patients</li> <li>AD</li> <li>No f/u</li> </ul>	CMAI-SF	CMAI-SF scores significantly decreased from 2 weeks onwards with 20%-45% improvement in agitation at 2 weeks $(p < .002)$ and 41.35% at 12 weeks $(p < .001)$ .	moderate
de Vasconcelos Cunha et al. 2007 (64)	Venlafaxine 37.5-131.25mg/d 6 weeks	Depression	<ul> <li>RCT</li> <li>31 patients</li> <li>Mild to moderate dementia with depression</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	MADRS	No significant difference in efficacy reported between venlafaxine and placebo.	strong
Greenwald et al. 1986 (65)	Trazodone 200-300mg/d plus adjunctive L-tryptophan 2.5g/d	VDB	<ul> <li>Single case study</li> <li>Moderately advanced dementia</li> <li>No f/u</li> </ul>	Observation	Reduction in screaming reported. No statistics reported.	case study
Lantz 2007 (66)	Citalopram 20mg/d combined with antibiotics, pain management, dental care, furniture re- arranging	VDB	<ul><li>Single case study</li><li>AD</li><li>No f/u</li></ul>	Observation	Reduction in screaming and calling out reported. No statistics reported.	case study
Lebert F, Stekke W et al 2004 (67)	Trazodone 50-300mg/day 12 weeks	Apathy BPSD	<ul> <li>Crossover RCT</li> <li>31 patients</li> <li>FTD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI	No significant improvement in apathy reported. Trazodone associated with statistically improved irritability, depression and agitation.	strong
Leo & Kim 1995 (68)	Clomipramine 50-150mg/d; 25-200mg/d	Disinhibition	<ul><li>2 case studies</li><li>No f/u</li></ul>	Observation	Sexually explicit behaviours reportedly reduced.	case studies
Lyketsos et al. 2000 (69)	Sertraline 25-150mg/d 12 weeks	Depression	<ul><li>RCT</li><li>22 patients</li><li>AD</li><li>Double-blinded</li><li>No f/u</li></ul>	CSDD HAM-D	Significantly reduced severity of mean scores for depressive symptoms reported on CSDD at weeks 3 and 12.	strong

Lyketsos et al. 2003 (70)	Sertraline 25-150mg/d 12 weeks	Depression	<ul> <li>RCT</li> <li>44 patients</li> <li>AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	CSDD HAM-D	Significantly greater reduction in depression reported for sertraline when compared to placebo as measured on CSDD ( $p = .002$ ) and HAM-D ( $p = .011$ ).	moderate
Magai et al. 2000 (71)	Sertraline 25-100mg/d 8 weeks	Depression	<ul> <li>RCT</li> <li>31 female patients</li> <li>Late-stage AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	CSDD CMAI	Reported decrease in depressive symptoms in both groups across time but no significant differences reported between groups.	strong
Mizukami et al. 2009 (72)	Milnacipran 15-75mg/d 12 weeks	Anxiety	<ul> <li>Open label, repeated measures design</li> <li>14 patients</li> <li>AD with major depressive episodes</li> <li>No f/u</li> </ul>	HAM-D	Significant decrease in anxiety (psychic) item of HAM-D reported ( $p = .0045$ ) for Milnacipran. No significant change reported for anxiety (somatic).	moderate
Petracca et al. 2001 (73)	Fluoxetine 10-40mg/d 6 weeks	Depression	<ul> <li>RCT</li> <li>41 patients</li> <li>AD with depression</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	HAM-D	No significant differences reported between treatment and placebo in HAM-D scores.	strong
Pollock et al. 1997 (74)	Citalopram 10-20mg/d 17 days	VDB BPSD	<ul> <li>Repeated measures design</li> <li>16 patients</li> <li>AD with agitation or psychotic symptoms without depression</li> <li>No f/u</li> </ul>	NBRS	No significant reduction in VDB reported.  Significant reductions in total NBRS scores reported across time for citalopram.	moderate
Pollock et al. 2002 (75)	Citalopram 10-20mg/d Perphenazine 0.05-0.1mg/kg/d 17 days	Apathy BPSD	<ul> <li>RCT</li> <li>85 patients:         citalopram n = 31         perphenazine n = 33         placebo n = 21</li> <li>AD/VaD/mixed/other with         agitation or psychotic         symptoms</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NBRS	No significant improvement reported in apathy scores from baseline.  Those treated with citalopram or perphenazine showed statistically significant improvement on agitation and psychosis NPI subscale scores. No significant changes in any factor reported for placebo.	strong

Pollock et al. 2007 (76)	Citalopram 10-40mg/d Risperidone 0.5-2mg/d 12 weeks	Agitation Psychotic symptoms	<ul> <li>RCT</li> <li>103 patients</li> <li>AD/VaD/DLB/mixed/other with agitation or psychosis</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NBRS	Reduced agitation and psychosis scores reported for citalopram across time and reduced psychosis scores reported for risperidone.  No significant differences reported in change for agitation or psychosis scores on NBRS.	strong
Raji et al. 2000 (77)	Citalopram 20mg/d 9 months	Disinhibition	<ul> <li>Single case study</li> <li>AD with sexual aggressiveness</li> <li>No f/u</li> </ul>	Observation	Reduction in disinhibited behaviours reported within a week of commencing citalopram. Symptoms in remission 9 months later, on treatment.	case study
Rosenberg et al. 2010 (78)	Sertraline 50-100mg/d 12 weeks	Depression	<ul> <li>RCT</li> <li>131 patients</li> <li>AD with depression</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	CSDD	No significant difference reported between sertraline and placebo.	moderate
Siddique et al. 2009 (79)	Citalopram 5-30mg/d 36 weeks	Psychotic symptoms BPSD	<ul> <li>Retrospective analysis of RCT with open-label phase</li> <li>44 patients</li> <li>AD</li> <li>No f/u</li> </ul>	NPI	Significantly reduced hallucinations reported ( $p = .022$ ) although frequency and intensity of symptoms were low at baseline. No significant effects reported for delusions. Reduced irritability reported.	moderate
Simpson & Foster 1986 (80)	<b>Trazodone</b> 100-500mg/d	Disinhibition	<ul><li>Case series</li><li>4 patients</li><li>Dementia</li><li>No f/u</li></ul>	Observation	Trazodone prescribed following ineffective treatment with neuroleptics. Disinhibited behaviours improved substantially.	case series
Stewart & Shin 1997 (81)	Paroxetine 20mg/d 3 months	Disinhibition	<ul><li>Single case study</li><li>Dementia</li><li>No f/u</li></ul>	Observation	Reduced disinhibited behaviour within 1 week and improvements sustained at 3 months, on treatment.	case study
Tosto et al. 2008 (82)	<b>Citalopram</b> 40mg/d	Disinhibition	<ul> <li>Single case study</li> <li>AD with irritability and hypersexuality</li> <li>No f/u</li> </ul>	Observation	Disinhibited behaviours largely reduced after 60 days and effects were ongoing at 12 months, on treatment.	case study
Psychostimula	nt					
Herrmann et al. 2008 (83)	Methylphenidate 10-20mg/d 5 weeks	Apathy	<ul> <li>Crossover RCT</li> <li>25 patients</li> <li>Mild to moderate AD with apathy</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	AES NPI	Greater improvement on AES.scores reported with methylphenidate when compared to placebo	strong

Other pharma	cological treatments					
Alkhalil et al. 2003 (84)	Gabapentin 300-900mg/d 6 months	Disinhibition	<ul><li>Single case study</li><li>AD with inappropriate sexual behaviour</li><li>No f/u</li></ul>	Observation	Disinhibited behaviour resolved and remained stable at 6 months, on treatment.	case study
Bodick et al. 1997 (85)	Xanomeline 25-75mg/3 x d 6 months	VDB BPSD	<ul> <li>RCT</li> <li>343 patients</li> <li>Mild to moderate AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	ADSS – vocal outbursts NOSGER	Dose dependent reduction in vocal outbursts reported ( $p \le .002$ ). A near significant reduction reported for NOSGER – disturbing behaviour ( $p = .05$ ) for 75mg treatment group when compared to placebo.	moderate
Bodick et al. 1997 (86)	Xanomeline 75-225mg/3 x d 6 months	VDB	<ul> <li>RCT</li> <li>343 patients: 75mg n = 85 150mg n = 84 225mg n = 87 placebo n = 87</li> <li>Mild to moderate AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	ADSS – vocal outbursts NOSGER	Dose dependent reduction in vocal outbursts reported ( $p \le .002$ ). A near significant reduction reported for NOSGER – disturbing behaviour ( $p = .05$ ) for 225mg treatment group when compared to placebo.	moderate
Bolea- Alamanac et al. 2011 (87)	Cyproterone acetate 100mg/d	Aggression	<ul><li>Single case study</li><li>Late-stage AD</li><li>No f/u</li></ul>	Observation	Reduced aggressive behaviour reported within first month of initiation of cyproterone acetate. The patient was less resistant to care and less argumentative.	case study
Cooper 1987 (88)	Medroxy- progesterone acetate 300mg IM/week 1 year	Disinhibition	<ul><li>Case series</li><li>4 patients</li><li>Dementia</li><li>1 year f/u</li></ul>	Observation	Disinhibited sexual behaviours ceased within 2 weeks of initiating treatment. 1 patient relapsed, to a lesser degree, on cessation of treatment after 1 year. Behaviour managed by "firm nursing". All patients' behaviour remained manageable at 1 year f/u.	case series
Dolder & McKinsey 2010 (89)	<b>Divalproex sodium</b> 125-1000mg/d 1 year	Agitation	<ul><li>Case series</li><li>20 patients</li><li>AD</li><li>No f/u</li></ul>	CGI-I	65% of patients reportedly responded to treatment.	case series

Dowling et al. 2008 (90)	Melatonin and bright light 5mg melatonin with >2500lux bright light in gaze direction for 1h/d 10 weeks	ND	•	RCT 50 patients: light + melatonin (LM) n = 15 light + placebo (LP) n = 18 control n = 17 AD with rest-activity rhythm disruption Double-blinded No f/u	Actigraphy	Daytime sleep significantly decreased in the LM group ( $p < .001$ ) and increased in the control group ( $p = .004$ ).  Total daytime activity significantly increased in the LM group ( $p = .04$ ) and decreased in the LP and control groups ( $p = .007$ and $p = .01$ ).  Day/night sleep ratio improved in the LM group ( $p < .001$ ) but no effect on night-time sleep variables reported.	moderate
Forester et al. 2007 (91)	Divalproex sodium 250-1500mg/d 6 weeks	Aggression Agitation VDB BPSD	•	Prospective, open-label study 15 patients: divalproex sodium monotherapy n = 7 combination therapy with atypical antipsychotics n = 8 Dementia with behavioural disturbances No f/u	CMAI NPI-NH	Significant reductions reported for physically aggressive behaviours at 3 ( $p < .01$ ) and 6 weeks ( $p < .05$ ) and in physically non-aggressive and verbally agitated behaviours at 1 ( $p < .01$ ) and 3 weeks ( $p < .01$ ) from baseline scores on CMAI.  Significant reductions also reported for agitation/aggression ( $p = .03$ ), disinhibition ( $p < .01$ ) and irritability/lability ( $p = .005$ ) subscales from baseline scores on NPI-NH.  Significant reductions reported for total CMAI at 1, 3 and 6 weeks when compared to baseline ( $p < .01$ ).  No significant differences reported between monotherapy and combination therapy.	moderate
Freund-Levi et al. 2008 (92)	Omega-3 supplement 430mg docosahexaenoic acid (DHA) and 150mg eicosapentaenoic acid (EPA) 12 months	Agitation Psychotic symptoms BPSD	•	RCT 174 patients AD Double-blinded No f/u	NPI MADRS	Significant reductions reported for NPI hallucinations ( $p$ = .04) and irritability ( $p$ = .008).scores in treatment group when compared to placebo at 6 months.  Significantly greater reductions reported for NPI agitation scores in those in treatment group with APOE4 allele ( $p$ = .006).  No significant differences were found between groups for NPI total scores at 6 or 12 months.	strong

Freymann et al. 2005 (93)	Carbamazepine 200mg/d	Disinhibition	<ul> <li>Single case study</li> <li>Moderate dementia with sexual disinhibition</li> <li>No f/u</li> </ul>	Observation	Disinhibited sexual behaviour remitted within three weeks.	case study
Gehrman et al. 2009 (94)	Melatonin 8.5mg immediate release and 1.5mg sustained release 10 days	ND Agitation	<ul> <li>RCT</li> <li>41 patients:     melatonin n = 24     placebo n = 17</li> <li>AD</li> <li>Double-blinded</li> <li>5 day f/u</li> </ul>	Actigraphy ABRS CMAI	No significant difference in treatment effects reported on any actigraphic parameters or CMAI ratings.	moderate
Hayashi et al. 2010 (95)	Yokukansan (TJ-54) 7.5g/d 4 weeks	Anxiety Psychotic symptoms BPSD	<ul> <li>Open-label study</li> <li>26 patients</li> <li>AD / mixed</li> <li>No f/u</li> </ul>	NPI	No significant reductions in NPI subscale scores reported, however clinically relevant reductions are reported for hallucinations, agitation/aggression, anxiety, apathy and irritability/lability.  Significant decrease in mean total NPI score reported ( <i>p</i> =0.0009).	moderate
Herrmann et al. 2007 (96)	Valproate 250-1500mg/d 6 weeks each	Aggression Agitation	<ul> <li>Crossover RCT</li> <li>14 patients</li> <li>Moderate to severe AD with BPSD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI CMAI	Significantly increased agitation reported for valproate when compared to placebo (NPI agitation/aggression, $p = .043$ ; CMAI, $p = .039$ ). A significant increase in agitation across time (CMAI, $p = .009$ ) also reported for valproate.	strong
Huertas et al. 2007 (97)	Cyproterone 100mg/d vs Haloperidol 2mg/d 105 days	Aggression	<ul> <li>Randomised, parallel-group study</li> <li>27 patients</li> <li>AD with aggression</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	SOAS	Significantly greater percentage of responders and those in remission reported for cyproterone ( $p = .0009$ ) than haloperidol ( $p = .012$ ).	strong

Husebo et al. 2011 (98)	Paracetamol max dose 3g/d Morphine max dose 20mg/d Buprenorphine max dose10µg/d Pregabaline max dose 300mg/d according to stepwise protocol as per assessed pain needs 8 weeks	Agitation BPSD	<ul> <li>RCT</li> <li>352 NH residents</li> <li>Moderate to severe dementia with clinically significant behavioural disturbances</li> <li>4-week f/u</li> </ul>	CMAI NPI-NH	Treatment of pain resulted in a significant reduction in agitation in intervention group when compared to control group ( <i>p</i> < .001) after 8 weeks.  Treatment of pain significantly decreased overall severity of BPSD.	strong
Iwasaki et al. 2005 (99)	Yi-Gan San (TJ-54) 7.5g/d 4 weeks	Psychotic symptoms Anxiety BPSD	<ul> <li>RCT</li> <li>52 patients</li> <li>AD/VaD/ DLB/AD with cerebrovascular disease</li> <li>Single-blinded</li> <li>No f/u</li> </ul>	NPI	Significant reductions reported in total NPI, hallucinations, agitation/aggression, irritability/lability and aberrant motor activity subscale scores ( $p < .05$ ). However, groups were not equal on outcome measures at baseline.	moderate
Kimura et al. 2009 (100)	Yokukansan (TJ-54) 7.5g/d 1-2 weeks	Aggression Agitation BPSD	<ul><li>Case series</li><li>5 patients</li><li>FTD</li><li>No f/u</li></ul>	NPI	Improvements on mean NPI total scores, delusions, agitation/aggression, apathy/indifference, disinhibition, irritability and aberrant motor behaviour reported.  Statistical significance not reported.	case series
Kyomen et al. 1991 (101)	<b>Diethylstilbestrol</b> 1mg	Disinhibition/ Sexual aggression	<ul><li>Single case study</li><li>Dementia</li><li>No f/u</li></ul>	Observation	Sexually disinhibited behaviour ceased within 3 weeks.	case study
Light & Holroyd 2006 (102)	Medroxy- progesterone acetate (IM) 100-2000mg/month	Disinhibition	<ul> <li>Case series</li> <li>5 patients</li> <li>AD/VaD/mixed dementia with behavioural disturbance (with or without depression)</li> <li>No f/u</li> </ul>	Observation	Sexually disinhibited behaviour ceased immediately or within 2 weeks.	case series

Lothstein et al. 1997 (103)	Conjugated oestrogens Oral - 0.625mg/d Patch - 0.05 or 0.10mg/d Antiandrogen therapy Leuprolide (Lueteinizing hormone-releasing hormone agonist) — lowest possible effective dose Depo-Provera 100+mg	Disinhibition/ sexual aggression	<ul> <li>Case review</li> <li>39 geriatric outpatients</li> <li>Cognitive impairment (including dementia) and sexual disinhibition</li> <li>No f/u</li> </ul>	Observation	Where appropriate, treatment with SSRI medication was trialled as a first option. According to a treatment algorithm, where degree of risk was unacceptable, oestrogen or antiandrogen therapy was initiated.  NB: check State and Territory requirements for consent before initiating treatment.  Where oral compliance could not be guaranteed, patches or injections were prescribed. 38/39 patients showed a marked improvement in sexually disinhibited behaviours. Sexually aggressive behaviours typically required	case review
Mahlberg & Walther 2007 (104)	3 years  Melatonin 3mg vs  Dronabinol 2mg vs  placebo	Agitation BPSD	<ul> <li>Placebo-controlled study</li> <li>24 patients:         melatonin n = 7         dronabinol n = 7         placebo n = 10</li> <li>AD with agitated behaviour</li> <li>No f/u</li> </ul>	Actigraphy NPI	oestrogen or antiandrogen therapy. Significant reductions reported in agitation $(p = .032)$ and ND $(p = .001)$ subscale scores as well as NPI total $(p = .043)$ for treatment group when compared to baseline. No significant changes reported for placebo group.	moderate
Mizukami et al. 2009 (105)	Yokukansan (TJ-54) 22.5g/d 8 weeks	Aggression Anxiety Psychotic symptoms BPSD	<ul> <li>Randomised crossover study</li> <li>106 patients</li> <li>AD/mixed dementia/DLB</li> <li>No f/u</li> </ul>	NPI	Significantly reduced mean subscale scores reported for agitation/aggression, irritability/lability, hallucinations, delusions, dysphoria, anxiety and NPI total scores during treatment periods but not nontreatment periods ( <i>p</i> < .05).	moderate
Okahara et al. 2010 (106)	Yokukansan (TJ-54) with donepezil 22.5g/d 4 weeks	Aggression BPSD	<ul> <li>Randomised, parallel-group study</li> <li>61 patients</li> <li>AD/mixed</li> <li>No f/u</li> </ul>	NPI	Significantly greater reduction in mean agitaiton/aggression and irritability/lability subscale scores as well as NPI total score in treatment group (Donepezil with Yokukansan) when compared to control group (Donepezil only) at week 4 (p < .05).	moderate
Ott 1995 (107)	Leuprolide (IM) 7.5mg/month	Disinhibition	<ul> <li>Single case study</li> <li>Frontal lobe dementia with hypersexuality</li> </ul>	Observation	Disinhibited sexual behaviour reportedly declined after 2 months and was almost completely remitted after the third injection.	case study

Passmore 2008 (108)	Nabilone 0.5-1mg/d 6 weeks	Agitation	<ul> <li>Single case study</li> <li>AD with behavioural disturbances</li> <li>No f/u</li> </ul>	Observation	Prompt reduction in levels of agitation and resistance to care reported on nabilone initiation. Resistance to care improved further with dosage increase. Symptoms remained controlled at 3 months, on treatment.	case study
Riemersma- van der Lek et al. 2008 (109)	Melatonin and bright light 2.5mg melatonin with whole day bright light (1000lux) Up to 3.5 years	ND BPSD	<ul> <li>RCT</li> <li>189 patients: light + melatonin n = 49 light only n = 49 melatonin only n = 46 double placebo n = 45</li> <li>92% dementia; AD/VaD/FTD/ DLB/PDD/Wernicke- Korsakoff/other</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	Actigraphy CSDD	Light only significantly increased total sleep duration ( $p$ = .04) and decreased depressive symptoms ( $p$ = .02).  Melatonin only significantly decreased sleep onset latency ( $p$ = .02), increased total sleep duration ( $p$ = .004) and increased duration of uninterrupted sleep epochs. Melatonin, however negatively impacted on mood.  Combined treatment improved sleep efficiency, nocturnal restlessness and duration of awakenings as well as decreased agitation (all $p$ = .01).	strong
Sato et al. 2007 (110)	Tandospirone 10-30mg/d 8 weeks	Anxiety Psychotic symptoms BPSD	<ul> <li>Open-label study</li> <li>13 patients</li> <li>AD/VaD with treatment-resistant BPSD</li> <li>No f/u</li> </ul>	NPI	Significant reduction reported in subscale scores for agitation/aggression ( $p < .01$ ), depression/dysphoria ( $p < .05$ ), anxiety ( $p < .05$ ) and irritability/lability ( $p < .01$ ).	moderate
Scripnikov et al. 2007 (111)	Ginkgo biloba Extract (EGb 761) 240mg/d 22 weeks	Anxiety Psychotic symptoms ND BPSD	<ul> <li>Placebo-controlled RCT</li> <li>400 patients; group numbers not reported</li> <li>AD/ VaD/AD with cerebrovascular disease</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI	Significant improvements reported on subscale scores for for apathy/indifference, anxiety, sleep/nighttime behaviour, irritability/lability and depression ( <i>p</i> < .001).	moderate

Shinno et al. 2008 (112)	Yokukansan (TJ-54) 7.5g/d 4 weeks	Anxiety Aggression Psychotic symptoms ND BPSD	<ul> <li>Repeated measures design</li> <li>5 patients</li> <li>AD/DLB</li> <li>No f/u</li> </ul>	NPI-NH Polysom- nography PSQI	Significant reductions reported on subscale scores for delusions ( $p < .01$ ), anxiety ( $p < .05$ ), hallucinations ( $p < .05$ ) and agitation/aggression ( $p < .05$ ) as well as NPI total ( $p < .01$ ) for Yi-Gan San when compared to baseline.  Significant improvements reported in total sleep time ( $p < .01$ ), sleep efficiency ( $p < .01$ ), stage 2 non-REM sleep ( $p < .01$ ), number of awakenings ( $p < .05$ ) and Periodic Limb Movements Index ( $p < .05$ ) on polysomnography as well as PSQI score ( $p < .05$ ).	moderate
Sival et al. 2002 (113)	Sodium valproate 480mg/d 3 weeks each	Apathy BPSD	<ul> <li>Crossover RCT</li> <li>39 patients; group numbers not reported</li> <li>AD/mixed/VaD/PDD/other dementia with aggressive behaviour</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	GIP	Significant reduction reported in restlessness ( $p = .02$ ), melancholic behaviour ( $p = .04$ ) and anxiety ( $p = .01$ ).	strong
Sommer et al. 2009 (114)	Oxcarbazepine 300-900mg/d 8 weeks	Aggression Agitation	<ul> <li>RCT</li> <li>103 patients</li> <li>AD/VaD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	NPI-NH BARS (Norwegian)	No significant differences reported between treatment and control groups on NPI-NH total score, agitation/aggression subscale score or BARS.	strong
Summers 2006 (115)	Propranolol 120 -180mg/d 1 year	Agitation	<ul><li>Single case study</li><li>Late-stage AD</li><li>No f/u</li></ul>	Observation	Agitation reportedly reduced by cessation of antipsychotics and commencement of propranolol. Symptoms remained stable for 1 year.	case study
Tune & Rosenberg 2008 (116)	<b>Divalproex</b> 2000mg/d	Disinhibition	<ul> <li>Single case study</li> <li>Dementia (AD or FTD, unconfirmed)</li> <li>No f/u</li> </ul>	Observation	Disinhibited behaviours continued although the medication "slowed him down".	case study

Walther et al. 2006 (117)	<b>Dronabinol</b> 2.5mg/d 2 weeks	Agitation Psychotic symptoms ND BPSD	•	Open-label study 6 patients AD/VaD No f/u	NPI Actigraphy	Significant reduction reported in subscale scores for agitation ( $p = .042$ ), aberrant motor behaviour ( $p = .042$ ) and night-time behaviours ( $p = .042$ ) as well as NPI total score ( $p = .027$ ) and nocturnal motor activity ( $p = .028$ ) when compared to baseline.	moderate
Wang et al. 2009 (118)	Prazosin 1-6mg/d 8 weeks	Aggression Agitation BPSD	•	RCT 22 patients AD with agitation/aggression Double-blinded No f/u	CGI-C NPI BPRS	Significantly greater reductions in treatment group on all outcome measures when compared to placebo. CGI-C, $p = .011$ ; NPI, $p = .012$ ; BPRS, $p = .036$ .	case study
Weiner et al. 1992 (119)	Medroxy- progesterone acetate 200mg/fortnight	Disinhibition	•	Single case study AD with hypersexuality No f/u	Observation	Disinhibited behaviours improved within 2 weeks.	case study
Wiseman et al. 2000 (120)	Cimetidine 600-1600mg/d Ketoconazole 100-200mg/d Spironolactone 75mg/d	Disinhibition	•	Chart review 20 patients Dementia with hypersexual behaviour No f/u	Observation	14/20 patients responded to cimetidine. 6/20 patients responded to combination of cimetidine with ketoconazole, spironolactone or both. Response time ranged between 1 and 8 weeks.	chart review
Brain Stimulati	•	T = .			T	T.,	T
Bentwich et al. 2011 (121)	Transcranial magnetic stimulation with cognitive training 1200 pulses/d 6 weeks of daily intensive treatment plus 3 months maintainence treatment	Depression	•	Repeated measures design 8 patients Mild to moderate AD No f/u	HAM-D	No significant reduction in depressive symptoms reported on the HAM-D.	moderate
Hausner et al. 2011 (122)	Electroconvulsive therapy >2.5x seizure threshold for unilateral and >1.5x seizure threshold for bilateral 6 weeks	Depression	•	Open-label study 44 patients 12 with mild to moderate AD 6-month f/u	HAM-D	Depressive symptoms almost completely remitted at 6-month f/u.	moderate

Scherder et al. 2006 (123)	Cranial electrostimulation 100Hz 30min/d x 5 days 6 weeks	ND	<ul><li>RCT</li><li>20 patients</li><li>Moderate to severe AD</li><li>6-week f/u</li></ul>	Actigraphy	No significant effect on rest-activity rhythm with high-frequency cranial electrostimulation.	case study
Sutor & Rasmussen 2008 (124)	Electroconvulsive therapy 6x seizure threshold for right unilateral and 1.5x seizure threshold for bilateral therapy	Aggression BPSD	<ul> <li>Retrospective chart review</li> <li>11 patients</li> <li>AD</li> <li>No f/u</li> </ul>	Patient charts	Reduced aggressive behaviour reported in 6 of 7 patients and clinical improvement in 1. Reduced VDB reported in 4 of 7patients and clinical improvement in 3. Reduced psychotic symptoms reported in 3 of 3 patients.	chart review
Van Dijk et al. 2006 (125)	Peripheral electrical nerve stimulation 160Hz 30min/d x 7 days 6 weeks	ND	<ul> <li>RCT</li> <li>62 patients</li> <li>AD</li> <li>Double-blinded</li> <li>No f/u</li> </ul>	Actigraphy	Nonsignificant trend toward improved interdaily stability and interdaily variability in intervention group. Treatment effects appeared to be evident in those <i>not</i> receiving concomitant ChEI therapy only.	case study

Notes: AD: Alzheimer's disease; VaD: vascular dementia; f/u: follow-up; BPSD: behavioural and psychological symptoms of dementia; CIBIC-plus: Clinician Interview-Based Impression of Change - plus carer interview; NPI: Neuropsychiatric Inventory; RCT: randomised controlled trial; NPI-D: Neuropsychiatric Inventory - Caregiver Distress Scale; VDB: vocally disruptive behaviour; BEHAVE-AD: Behavioural Pathology in Alzheimer's Disease; CGI-I: Clinical Global Impression - Improvement; CGI-S: Clinical Global Impression - Severity; DLB: dementia with Lewy bodies; CMAI: Cohen-Mansfield Agitation Inventory; CGI-C: Clinical Global Impression - change scale; ND: nocturnal disruption; PDD: Parkinson's disease dementia; REM: rapid eye movement; FTD: frontotemporal dementia; BPRS: Brief Psychiatric Rating Scale; BARS: Brief Agitation Rating Scale; CMAI-SF: Cohen-Mansfield Agitation Inventory - Short Form; PANSS-EC: Positive and Negative Syndrome Scale - Excited Component; ACES: Agitation Calmness Evaluation Scale; NPI-NH: Neuropsychiatric Inventory - Nursing Home Version; GDS: Geriatric Depression Scale; MADRS: Montgomery - Asberg Rating Scale; CSDD: Cornell Scale for Depression in Dementia; HAM-D: Hamilton Rating Scale for Depression; NBRS: Neurobehavioural Rating Scale; AES: Apathy Evaluation Scale; CIBIC: Clinicians Interview-Based Impression of Change; ADSS: Alzheimer's Disease Symptomatology Scale; NOSGER: Nurses' Observation Scale for Geriatric Patients; ABRS: Agitated Behaviour Rating Scale; SOAS: Staff Observation Aggression Scale; PSQI: Pittsburgh Sleep Quality Index; GIP: Gedragsobservatieschaal voor de Intramurale Psychogeriatrie [Dutch Behavior Rating Scale for Psychogeriatric Inpatients]

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