

Editorial

Psychological treatment for depression and anxiety associated with dementia and mild cognitive impairment†

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**Summary**

Depression and anxiety are commonly associated with cognitive impairment. A systematic review of psychological treatments that appears in this issue of the Journal highlights the current paucity of good-quality data, but suggests these interventions hold promise. Given the increasing burden of dementia in our community, novel adequately powered randomised controlled trials in this area are urgently needed.

Declaration of interest

None.

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Background

Dementia and cognitive impairment are major public health issues of the 21st century. In 2005 more than 24 million people worldwide had dementia and this number is expected to double by 2025.¹ Depression and anxiety symptoms may affect as many as 50% of people with dementia and mild cognitive impairment (MCI) during the course of the illness,² further compromising the quality of life of patients and increasing burden of care and costs. Antidepressants are frequently used in the management of these patients, but their efficacy is equivocal and may expose those treated to unwanted side-effects.³ The role of psychological interventions in managing depression or anxiety associated with dementia remains unclear, but is consistent with existing guidelines advocating the use of non-pharmacological interventions as the first step in treating neuropsychiatric symptoms of dementia.⁴

Currents findings from the literature

In this issue of the *BJPsych*, Orgeta and colleagues⁵ systematically review available randomised controlled trials (RCTs) of psychological interventions for the treatment of depression and anxiety in people with dementia and with MCI. The review utilised a thorough and comprehensive search strategy, but yielded only six trials that included a total of 439 participants. All six studies contributed to the meta-analysis of depression but only two had available data on anxiety. The authors reported a beneficial effect for psychological interventions on depression with little evidence of statistical heterogeneity. Psychological interventions reduced clinician-rated anxiety but had no effect on

individual self-ratings. The intervention had no effect on secondary outcomes, although the review probably lacked power.

The use of exit data (i.e. scores on rating instruments at the completion of the respective trials) rather than change from baseline scores and the restriction of the meta-analyses to complete case analyses are notable limitations, as is the absence of trials for people with MCI. The somewhat limited number and quality of the trials included in the analyses also raises concerns about the external validity of the findings. Nonetheless, the results reported by Orgeta and colleagues are important in this relatively under-researched area, particularly when one considers the paucity of demonstrably effective treatments.

A well-powered multicentre trial of the antidepressants sertraline and mirtazapine for the treatment of depression associated with dementia failed to show any benefit of treatment.⁶ The authors randomly assigned 326 people with Alzheimer's disease and depression to treatment with sertraline ($n=107$, up to 150 mg daily), mirtazapine ($n=108$, up to 45 mg daily) or placebo ($n=111$). A total of 39 weeks of follow-up data were available. Treatment with antidepressants did not reduce depression scores relative to placebo after 13 or 39 weeks of treatment, but both sertraline and mirtazapine were associated with greater frequency of adverse reactions compared with placebo (43%, 41% and 26%, respectively). Interestingly, all participants showed a lessening of depressive symptoms during the treatment period, suggesting a tendency to natural recovery over time and possibly a non-specific effect of the intervention. A similar non-specific effect of psychological interventions could potentially account for the findings reported by Orgeta and colleagues.⁵

The potential antidepressant effect of other types of interventions should also be considered. Physical activity decreases the severity of depressive symptoms in cognitively intact populations⁷ although benefits in those with established cognitive impairment is less clear. Lautenschlager and colleagues⁸ investigated the effect of a 24-week physical activity programme compared with control conditions in 170 participants with memory complaints with or without cognitive impairment. The authors found that physical activity had a positive effect on cognitive function (absolute difference between intervention and control groups of -1.3 points, 95% CI -2.38 to -0.22) but no obvious effect on depressive symptoms measured with the self-report Beck Depression Inventory (-0.94 for the intervention *v.*

†See pp. 293–298, this issue.

–0.75 for controls, $P=0.44$). These results may have been because of the fact that the volunteers with clinically significant symptoms of depression were excluded from this and other similar trials.⁹ Hence, it remains to be established whether physical activity will have a role to play in the management of people with depression (and possibly anxiety) associated with dementia.

Various other non-pharmacological approaches have been investigated for the treatment of neuropsychiatric symptoms associated with dementia, but few have focused on anxiety or depression.¹⁰ These have included reminiscence therapy, validation therapy, music therapy, reality orientation, cognitive stimulation and interventions with carers. The results suggest a modest beneficial effect of behavioural strategies.¹⁰ A recent RCT investigating the effect of a 12-week home-based problem adaptation therapy (PATH) for depression provides further evidence in support of psychological and behavioural therapies.¹¹ The authors enrolled 74 individuals and found a positive effect for depression in the PATH group compared with supportive therapy (Cohen's $d=0.60$, 95% CI 0.13–1.06, $P=0.005$). The PATH group also had significantly greater rates of remission of depressive symptoms compared with the control group (37.8% *v.* 13.5%, $P=0.02$).

Recently, cognitive bias modification (CBM) has emerged as another possible form of treatment for this population. CBM is a novel and simple intervention that targets attentional and interpretative biases associated with anxiety, dysphoria and depression. CBM uses implicit memory systems, which are spared until late in the course of dementia. CBM is effective at reducing depressive symptoms in adults without cognitive impairment and holds promise as an effective form of treatment for people with depression in dementia. This intervention has not previously been subjected to rigorous clinical trials in this population, but an RCT is currently under way.¹²

The prevalence of anxiety and depressive symptoms in people with cognitive impairment will continue to increase with the ageing of our society. It is essential that we develop clear, evidence-based treatment options that are well tolerated with minimal risk of adverse effects. Psychological therapies may assist with the management of this major clinical problem, although supportive evidence is not particularly compelling at this stage. The systematic review by Orgeta and colleagues provides a useful summary of available trials, but novel adequately powered RCTs are needed.

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References

- 1 Ferri CP, Prince M, Brayne C, Brodaty H, Fratiglioni L, Ganguli M, et al. Global prevalence of dementia: a Delphi consensus study. *Lancet* 2005; **366**: 2112–7.
- 2 Lyketsos CG, Lopez O, Jones B, Fitzpatrick AL, Breitner J, DeKosky S. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: results from the cardiovascular health study. *JAMA* 2002; **288**: 1475–83.
- 3 Nelson JC, Devanand DP. A systematic review and meta-analysis of placebo-controlled antidepressant studies in people with depression and dementia. *J Am Geriatr Soc* 2011; **59**: 577–85.
- 4 National Institute for Health and Care Excellence. *Dementia: Supporting People with Dementia and their Carers in Health and Social Care. Clinical Guideline 42*. NICE, 2006.
- 5 Orgeta V, Qazi A, Spector A, Orrell M. Psychological treatments for depression and anxiety in dementia and mild cognitive impairment: systematic review and meta-analysis. *Br J Psychiatry* 2015; **207**: 293–8.
- 6 Banerjee S, Hellier J, Dewey M, Romeo R, Ballard C, Baldwin R, et al. Sertraline or mirtazapine for depression in dementia (HTA-SADD): a randomised, multicentre, double-blind, placebo-controlled trial. *Lancet* 2011; **378**: 403–11.
- 7 Cooney GM, Dwan K, Greig CA, Lawlor DA, Rimer J, Waugh FR, et al. Exercise for depression. *Cochrane Database Syst Rev* 2013; **9**: CD004366.
- 8 Lautenschlager NT, Cox KL, Flicker L, Foster JK, van Bockxmeer FM, Xiao J, et al. Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease: a randomized trial. *JAMA* 2008; **300**: 1027–37.
- 9 Forbes D, Thiessen EJ, Blake CM, Forbes SC, Forbes S. Exercise programs for people with dementia. *Cochrane Database Syst Rev* 2013; **12**: CD006489.
- 10 Livingston G, Johnston K, Katona C, Paton J, Lyketsos CG, Old Age Task Force of the World Federation of Biological Psychiatry. Systematic review of psychological approaches to the management of neuropsychiatric symptoms of dementia. *Am J Psychiatry* 2005; **162**: 1996–2021.
- 11 Kiosses DN, Ravdin LD, Gross JJ, Raue P, Kotbi N, Alexopoulos GS. Problem adaptation therapy for older adults with major depression and cognitive impairment: a randomized clinical trial. *JAMA Psychiatry* 2015; **72**: 22–30.
- 12 Almeida OP, MacLeod C, Flicker L, Ford A, Grafton B, Etherton-Beer C. Randomised controlled trial to improve depression and the quality of life of people with Dementia using cognitive bias modification: RAPID study protocol. *BMJ Open* 2014; **4**: e005623.