Behavioural and psychiatric symptoms in people with dementia admitted to acute hospitals

We would like to commend Sampson et al. on undertaking the difficult task of identifying and monitoring behavioural and psychological symptoms of dementia (BPSD) in people admitted to acute medical wards. The authors have also done their best to untangle the BPSD syndrome from similar clinical symptomatology seen in delirium, which still remains an ongoing conundrum for many of us working in liaison psychiatry. The study not only provides a wealth of information, but also raises a number of issues about how BPSD presentation might differ in older people when admitted to acute medical settings and how it influences their outcomes.

The authors used the Behavioral Pathology in Alzheimer’s Disease scale (BEHAVE-AD), which has been widely used to detect behavioural problems in people with dementia, in particular Alzheimer’s disease. However, this scale has a number of shortcomings, neglecting some important symptoms of dementia, such as apathy, irritability and/or disinhibition, that are frequently present in dementia. The low–medium BPSD scores (2.6–4.4 mean BEHAVE-AD severity) are somewhat surprising, since the majority of the enrolled participants had higher Functional Assessment Staging Test (FAST) staging, corresponding to more advanced stages of dementia. The low–medium BPSD scores are usually associated with mild cognitive impairment. Only five individuals coming from an ‘other’ place of residence (continuing NHS care?) had substantially higher BPSD severity scores. Similarly, the severity of the dementia (as measured via the FAST) did not influence BPSD scores, suggesting that either the medical problems modified the BPSD presentation, or the BPSD were pharmacologically managed. The only factor to have a significant effect on BPSD was presence of delirium, thus highlighting the difficulties in routine clinical settings of differentiating between BPSD and clinical symptoms of delirium.

Nevertheless, Sampson et al.’s work undoubtedly indicates that hospitals make people with dementia worse, trebling their paranoia and delusional beliefs, causing hallucinations, making them more aggressive and disturbed, and substantially worsening their moods and anxieties. These findings support the public’s widespread beliefs that hospitals are dangerous places, not only filled with sick people and germs, but with a wide potential for something to go amiss in lieu of wrong. And this ‘wrong’ ranges from having newly acquired diagnosis of dementia when physically unwell to worsening BPSD, further complicating their polypharmacy and making them more frail and with poorer functional outcomes, as well as increasing their likelihood of death. Not surprisingly, this also affects their formal and informal caregivers. There is a striking discord between the severity of the recorded BPSD and the caregiver’s distress, arguing that the problems around the escalating in-hospital behavioural changes are much more serious than the physical illness itself.

Many of the highlighted BPSD could be easily regulated with non-pharmacological approaches, including better orientation, information and knowing our patients. What is happening to make our hospitals more dementia-friendly? A number of hospitals have already introduced dementia-friendly wards that should be fully equipped with the professional experts in dementia care. However, surprisingly, there is a void of research evidence regarding how the newly introduced dementia-friendly policy in acute medical settings influences the behaviour of people with dementia. Since most of the people with BPSD come from residential and nursing care, one wonders whether there should be another way of introducing dementia-friendly management. Perhaps an ‘in-home health dementia care’ approach would avoid (unnecessary) hospital admissions, and involve medical care professionals treating people with dementia in their own home whenever possible. This would reduce substantially not only the distress that both people with dementia and their caregivers face when in the acute medical setting, but also reduce hospital admissions, and thus result in substantial financial savings. The data from a recent study on people with advanced dementia stages prove that this can be successfully done, stressing that managing the distress, rather than behaviours that challenge, is central when treating people with dementia. We now need to take these lessons on board and implement them not only within our acute medical wards, but also adapt them to use in the community.


Author’s reply: Mukaetova-Ladinska & Scully’s comments on the challenges of conducting clinical research involving people with dementia on acute hospital wards raise the issue of whether BPSD may present differently in the acute hospital.

In our study, those with more severe dementia were unwell, often bed-bound, and may have been less able to display BPSD (e.g. wandering or pacing). Additionally, 12% of our cohort was taking an antipsychotic (details available from the authors on request), and many of these patients had more severe dementia. We note the problem of recall bias in staff who may report the ‘unknown’ safety concern for aripiprazole once monthly.

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those with severe dementia may not have been recognised. Although BPFD were not associated with severity of dementia assessed by the FAST,3 we notice a possible difference between those of stages 3–5 (mean total BEHAVE-AD score over admission: 2.4) and the more severe stages (means 3.6, 3.4 and 3.7, respectively, for stages 6a–c, 6d–e and 7a–f).

We agree the BEHAVE-AD scale has shortcomings; for example, it misses apathy and disinhibition.3 Our choice was pragmatic, based on ease of administration and available staff time. The Neuropsychiatric Inventory has more detailed items on agitation and aggression, but we also used the Cohen–Mansfield Agitation Inventory to characterise agitated behaviour (details available from the authors on request) and wished to avoid duplicating data collection. We would like to highlight that most of our cohort did not come from residential or nursing care; 67% were admitted from their own home (Table 2).1

Although admission is overall a negative experience, the precipitating illness may require hospital treatment. We had no data on BPFD prior to admission or how they would have evolved in another setting. Teasing out which elements of the admission have the strongest influence on poor outcomes, or whether the physical illness causing the admission produces negative effects, would require further investigation. Unfortunately, the answers to these questions will be complex and methodologically challenging to define properly.

There is recent evidence that improving the hospital environment for people with dementia is worthwhile.1 We hope our paper provides information to inform more effective interventions.

More data on speed of remission with ECT in geriatric depression

We appreciate the important contribution of Spans et al1 to the evidence that electroconvulsive therapy (ECT) is a rapidly acting treatment in geriatric depression. Their data are a reminder that, despite the recent excitement about other neuromodulation modalities for the treatment of depression, ECT remains a standard and vital treatment for our most seriously ill patients, particularly those in the geriatric age group. We would like to add data about the speed of ECT remission in geriatric depression from the ongoing National Institute of Mental Health (NIMH)-supported multicentre trial, Prolonging Remission in Depressed Elderly (PRIDE, ClinicalTrials.gov Identifier: NCT01028508).

Our group has just completed enrolment of 237 patients in phase 1 of a trial in which patients with unipolar depression over 60 years of age receive a course of ultra-brief pulse right unilateral ECT augmented with venlafaxine. (Phase 2 of the trial is random allocation to venlafaxine plus lithium or venlafaxine plus lithium plus flexible maintenance ECT. This phase of the trial will be completed in the next 3 months.) The cohort of 133 remitters in phase 1 required a mean of 7.3 (s.d. = 3.1) ECT sessions to reach remission, defined as a Hamilton Rating Scale for Depression (HRSD-24) score of <10 on two consecutive sessions (personal communication, R. Knapp). Because ECT was administered three times a week in our study, seven treatments approximate 2.5 weeks until remission, a time comparable to that reported by Spans et al.

In our previous study, comparing the efficacy of the three standard electrode placements in ECT,2 the mean number of ECT sessions needed to achieve remission in patients over 60 years of age was also consistently low: bi-temporal (5.5, s.d. = 2.2, n = 19), bi-frontal (5.4, s.d. = 2.1, n = 11), right unilateral brief pulse (5.1, s.d. = 2.1, n = 19). Speed of response takes on added importance when patients are urgently ill and present with severe suicidal urges, agitation, psychosis, or malnutrition from profound depression. Because of its unsurpassed efficacy and now better-documented speed of response in geriatric depression, ECT should no longer be relegated to last place in treatment algorithms for severe depression.3 Finally, it should be noted that in both Spans et al and the PRIDE study, newer techniques allow practitioners to prescribe ECT in a form that is more tolerable for patients than in the past.4


Correspondence

...effect size $d = 0.9$, $P = 0.071$, compared with the late remitters.

Our group has just completed the Mood Disorders in Elderly treated with Convulsive Therapy (MODECT) study, which included 110 patients with a mean age of 73 years (range 55–90 years). This study aims to identify predictors for the efficacy of ECT using neuroimaging, clinical measures (on cognition, mood and psychomotor symptoms), neuropsychological data and biological measurements. Recently, another research group in The Netherlands presented exciting data using a functional magnetic resonance imaging marker for the prediction of individual ECT outcome. The MODECT data provide a wonderful opportunity to study and possibly replicate these findings in an older cohort.

With respect to the optimal treatment modality, we agree that the speed of remission using ultra-brief pulse ECT in the PRIDE study was indeed comparable to the speed of remission of the merged ultra-brief/brief pulse ECT groups. However, the assessments of week 2 of the ECT group were neglected for comparison with the medication group. In the original ECT study, this elderly, brief pulse subgroup achieved remission significantly faster than the elderly, ultra-brief pulse subgroup: remission was achieved in 2.2 weeks (s.d. = 0.9) vs. 3.0 weeks (s.d. = 1.1; $t(29) = -2.249$, $P = 0.032$), respectively. This finding may denote the possibility that twice-weekly brief pulse ECT with either unilateral or bilateral electrode placement could have superior efficacy compared with ultra-brief pulse treatment.

The recent evidence shown by our research and the recent findings of the PRIDE study once more emphasise the clinical importance of ECT’s rapid effect; ECT should indeed be taken into account when revising treatment algorithms for severely depressed elderly patients, hence avoiding the use of the less effective and account when revising treatment algorithms for severely depressed patients.

The ‘unknown’ safety concern for aripiprazole once monthly

Fleischhacker et al report that treatment-emergent adverse effects are comparable for aripiprazole 400 mg once monthly and a suboptimal dose (50 mg) of aripiprazole once monthly.1 Also, they state that the ‘clinical relevance’ of statistically significant difference in Barnes Akathisia Rating Scale score with aripiprazole 400 mg once monthly against oral aripiprazole is ‘unknown’. Akathisia is known to be the most clinically relevant adverse effect with oral aripiprazole because of the subjective distress caused to the patient and the increased risk of agitation and suicide associated with it. Hence, a higher rate of akathisia with aripiprazole 400 mg once monthly cannot be discounted as being of ‘unknown clinical relevance’. Further, a deeper look at the apparently similar rates of ‘any treatment-emergent adverse effects’ for the two doses of aripiprazole reveals that the rates may not be similar if psychotic disorder and schizophrenia (which are efficacy outcomes and in no way can be considered as adverse effects for the purposes of this study) are removed from the list.

The article minimises the possible safety concerns associated with aripiprazole 400 mg once monthly. A precise assessment of safety concerns (besides efficacy) is of utmost importance for a potential prescriber and there is potential of a prescriber being misguided by superficially reading this article. Further, efficacy outcomes of the study could have been contaminated by the noticeably high and differential discontinuation rates in the two active arms. The last observation carried forward (LOCF) method used for analysis of missing data tends to underestimate worsening in intention-to-treat (ITT) analyses. A comparison of results generated by ITT and per protocol analysis could have been more informative in assessing the efficacy outcomes.

Authors’ reply: Gupta & Kamboj correctly note that akathisia is a clinically relevant adverse effect with oral aripiprazole because it causes distress and is associated with an increased risk of agitation and suicide in patients with schizophrenia. We did not want to discount a higher rate of akathisia with aripiprazole 400 mg once monthly as being of ‘unknown clinical relevance’, but rather questioned the clinical relevance of the absolute 0.11-point group difference on the 5-point Barnes Akathisia Global Scale. We appreciate that this could have been stated more clearly. In our study,1 10.6% of patients treated with aripiprazole 400 mg once monthly reported akathisia as a treatment-emergent adverse event (TEAE), as did 6.8% of patients treated with oral aripiprazole and 8.4% of patients treated with a sub-therapeutic dose of aripiprazole once monthly; no patients discontinued because of akathisia. Rates of agitation, reported as a TEAE, were low among all treatment groups (aripiprazole 400 mg: 2.6%; oral aripiprazole: 0.8%; aripiprazole 50 mg: 0%). As noted in our manuscript, Clinical Global Impression Severity of Suicide (CGI-S) scores and Columbia Suicide Severity Rating Scale (C-SSRS) suicidal ideation intensity total scores remained stable across treatment groups (see Table 4 in the published article).

Gupta & Kamboj note that the rate of TEAEs with aripiprazole 400 mg once monthly may not be similar to the rate with a sub-therapeutic dose of aripiprazole once monthly if psychotic disorder and schizophrenia are removed from the list of TEAEs. They also suggested that psychotic disorder and schizophrenia are not TEAEs and are efficacy outcomes. In this context, we note that the regulatory authorities in Europe and the USA require accurate...
recording of all patient-reported TEAEs, and psychotic disorder, psychotic symptoms, and schizophrenia are Medical Dictionary for Regulatory Activities (MedDRA)-defined adverse events and typical patient-reported TEAEs in antipsychotic trials.

Gupta & Kamboj also state that reporting efficacy outcomes using the LOCF method for an ITT analysis could be misleading because discontinuation rates differed between the two active treatment groups. Gupta & Kamboj recommend a comparison of ITT and per protocol results for a more informative assessment of efficacy outcomes in our 38-week trial. LOCF was not used for the primary efficacy outcome or for the additional efficacy outcomes. As reported in our paper, the Kaplan–Meier estimated impending relapse rate at week 26 (primary study endpoint, ITT population: aripiprazole 400 mg: 7.12%; oral aripiprazole: 7.76%; aripiprazole 50 mg: 21.80%) was similar to week 26 in the per protocol results (i.e. for observed impending relapse rates, aripiprazole 400 mg: 6.79%; oral aripiprazole: 7.14%; aripiprazole 50 mg: 18.32%).

Lastly, we trust that readers of the BJPsych do not base their treatment decisions on ‘superficial reading’.

Effects of a novel schizophrenia risk variant rs7914558 at CNNM2 on brain structure and attributional style. BJP, 204, 115–121. The authors named the risk allele at this locus as being the ‘A’ allele. The risk allele should have been named as the major ‘G’ allele. The mistake in naming the risk allele at this locus does not otherwise affect the results or their interpretation.

Relationship of suicide rates to economic variables in Europe: 2000–2011. BJP, 205, 486–496. The 31st author’s name is Ole Andreassen. The misspelling of this author’s name has been corrected post-publication, in deviation from print and in accordance with this correction.

Recovery-focused cognitive-behavioural therapy for recent-onset bipolar disorder: randomised controlled pilot trial. BJP, 206, 58–66. The curves in Fig. 3 were printed incorrectly as identical to those in Fig. 2. The correct figures are reproduced below.
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