Predictors of cognitive improvement after reality orientation in Alzheimer's disease

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Abstract

Background: there is increasing evidence to support the efficacy of reality orientation in cognitive deficits in patients with Alzheimer's disease. The clinical characteristics of patients who respond to reality orientation are poorly understood; this knowledge could be important, given that the provision of reality orientation therapy is labour-intensive and may provoke emotional distress.
Aim: to evaluate retrospectively which demographic and clinical characteristics of Alzheimer's patients predict cognitive outcomes.
Method: we analysed 38 mild-to-moderately demented outpatients who regularly attended a one-month formal reality orientation programme. The mini mental state examination score changes from baseline—and immediately after—reality orientation were correlated with demographic and pre-treatment clinical characteristics by a linear regression analysis.
Results: short-term responsiveness to reality orientation was significantly predicted by a lower level of cognitive functioning (as measured by the mini mental state examination) at baseline and by the absence of euphoria, accounting together for 57.6% of variance.
Conclusion: a lower mini mental state examination and the absence of euphoric behaviour in patients with mild-to-moderate Alzheimer's disease may predict a good cognitive outcome of reality orientation therapy.

Keywords: *Alzheimer's disease, euphoria, frontal lobe syndrome, predictor variables, reality orientation, short-term responsiveness*

Introduction

Reality orientation (RO) therapy is a cognition-oriented technique for dementia patients with memory loss and time-place disorientation [1, 2]. Its purpose is to re-orientate patients by means of continuous stimulation with repetitive orientation to the environment.

A recent meta-analysis of eight controlled trials of RO research [1] concluded that RO techniques should be considered as part of a more general dementia care programme, as they improve orientation and memory [3]. They also attenuate behavioural symptoms of dementia [2]. It is unclear how far the benefits of RO continue after the end of treatment, but a continued programme may be necessary to sustain potential benefits.

The clinical and neuropsychological features which predict the success of RO have not been investigated [4, 5].

We have attempted to evaluate which characteristics suggest short-term responsiveness to classroom-based RO over one month.

Materials and methods

Subjects

We enrolled consecutively 38 outpatients, according to the following criteria: a) clinical diagnosis of probable AD [6, 7]; b) presence of mild to moderate cognitive

impairment: Mini Mental State Examination (MMSE) score between 14 and 25 [7]; c) absence of clinically important behavioural symptoms, severe enough to interfere with the implementation of RO; and d) ability to attend regular RO sessions. They attended a one-month classroom-based RO at the day hospital of our Alzheimer Unit. This is a multidisciplinary care centre providing diagnostic evaluation and treatment of dementia.

Methods

A small homogenous group of four patients met daily, five days a week for one month. Each meeting lasted one h and was conducted by two RO therapists.

The method used by our therapists is described by Zanetti *et al.* [8]. It consists of repetitive stimulation of patients' autobiographical and semantic memory, attention, language and orientation. The group was encouraged to discuss different issues and patients were urged to voice their opinions and to engage with therapists.

Before RO began, all patients had a multidimensional evaluation, assessing the following domains: a) Overall cognitive functioning: MMSE [7]; b) Functional status: Instrumental and Basic Activities of Daily Living (as reported by the primary caregiver [9, 10]), Direct Assessment of Functional Status (DAFS) (an instrument which permits us to assess patients' functionality through the direct observation of their performance [11, 12]); c) Affective state: Geriatric Depression Scale [13]; and d) Behavioural symptoms: the Neuropsychiatric Inventory (NPI) [14, 15]. We grouped the NPI subscales into the 'mood' (anxiety, depression), 'psychotic' (delusions, hallucinations) and 'frontal' (euphoria, disinhibition) syndromes according to results of our previous study [16].

Two days after ending the RO programme, the MMSE was repeated to measure change from the baseline score.

Statistical analysis

We analysed data by applying the Statistical Package for Social Sciences [17]. Preliminary information on the relationship between the baseline evaluative measures and the magnitude of cognitive gain induced by RO were drawn from a Pearson's correlation analysis. Then a linear regression analysis was computed, taking the MMSE $t1$–$t0$ as a dependent variable and baseline measures with statistical significance after the Pearson's correlation analysis as regressors (i.e., independent variables). We then assessed which variables most influenced the magnitude of cognitive gain as indexed by the MMSE after RO. For the regression model, we used stepwise methods. We adjusted significant correlation coefficients for age, sex, years of education and concomitant drug treatment. We considered four classes of medications, assumed negatively (benzodiazepines, neuroleptics) or positively (serotoninergic

antidepressants, acetylcholinesterase inhibitors) to interfere with both cognition and affect in AD patients [18, 19]. Concomitant drug treatment remained unchanged during RO intervention.

Results

Clinical and socio-demographic characteristics of the RO trainees are summarised in Table 1. The sample is composed mainly of women (79%); only 4% of the sample was mildly depressed, as evaluated by GDS (cut-off $> 10/30$).

At baseline, the MMSE mean was 20.8 ± 3.2; at the end of RO training, a *t*-test for paired measures indicated a statistically significant improvement of patients' scores at MMSE (mean $= 1.73 \pm 3.5$, $P = 0.01$).

The preliminary Pearson's correlation analyses between the MMSE scores' changes and measures of functionality, affective status and behaviour are reported in Table 2. Following the linear regression analysis, only the MMSE at baseline and the item of euphoria belonging to the 'frontal' syndrome factor [16] independently accounted for most unique variance (57.6%) in the prediction of successful response to a short-term RO programme. In particular, these variables correlated

Table 1. Demographic and clinical characteristics of 38 Alzheimer's disease patients

	Means $\pm$ SD	Observed range
Age (years)	77 ± 8.2	
Women %	79%	–
Education (years)	6 ± 1.6	3–9
Functional status		
IADL (functions lost)	3.4 ± 3.3	0–8
BADL (functions lost)	0.5 ± 1.2	0–5
DAFS	59.3 ± 12.4	34–73
Depression symptoms		
GDS	7.7 ± 5.1	1–20
Behavioural profile		
NPI	23 ± 17	0–66
Delusions	2.6 ± 3.7	0–12
Hallucinations	0.6 ± 2	0–8
Agitation	2.6 ± 3.3	0–12
Depression/dysphoria	3.2 ± 2.9	0–12
Anxiety	2 ± 3.2	0–12
Euphoria/elation	2.3 ± 3	0–12
Apathy/indifference	4.2 ± 3.5	0–12
Disinhibition	1.1 ± 2.9	0–12
Irritability/lability	2.7 ± 3.8	0–12
Aberrant motor behaviour	2.7 ± 3	0–12
Behavioural syndromes		
Mood (anxiety, depression)	7 ± 11.5	0–15
Psychotic (delusions, hallucinations)	2.9 ± 3.8	0–12
Frontal (euphoria, disinhibition)	2 ± 4.6	0–24

SD, standard deviation; IADL, instrumental activities of daily life; BADL, basic activities of daily life; DAFS, direct assessment of functional status; GDS, geriatric depression scale; NPI, neuropsychiatric inventory.

Table 2. Correlation between cognitive changes as measured by mini mental state examination (mini mental state examination $t1$–$t0$) and patients' clinical characteristics (Pearson's coefficients)

	r	P
BADL	0.5	0.002
DAFS	−0.5	0.001
Baseline MMSE	−0.5	0.001
NPI total	−0.3	0.06
Anxiety	0.4	0.01
Euphoria	−0.6	<0.001
Frontal syndrome	−0.4	0.009

BADL, basic activities of daily life; DAFS, direct assessment of functional status; MMSE, mini mental state examination; NPI tot, neuropsychiatric inventory.

negatively; AD patients with initial low overall cognitive functioning, and with less pronounced euphoria, benefited most from attending a short-term RO programme.

Discussion

Our retrospective study, which tried to identify the clinical profile of AD patients most suited to RO, indicates that those who benefit most from short-term RO have an initial greater cognitive impairment, as measured by MMSE, and are not euphoric [14].

Our study suggests that patients with moderate dementia are more likely to improve than those with mild AD.

Some studies suggest that euphoria can disturb AD patients' attention and concentration, already impaired by the dementing process [20], and render them unlikely to benefit from RO. The prefrontal cortical area is involved in inhibition and control of affect [16]—important components of executive function—and their impairment in AD may negatively interfere with cognition-oriented therapy [21]. Frontal lobe syndrome is characterised by language impairment and its involvement in AD [22] can reduce the efficacy of RO, as this rehabilitative intervention relies mainly on verbal interactions.

Age, sex, level of formal education, depressive symptomatology and functional impairment did not predict responsiveness to RO. This suggests that socio-demographic characteristics of AD patients may play a small role in identifying suitable candidates for RO sessions. Moreover, neither initial depressive symptomatology, nor severe functional impairment, should exclude AD patients from RO programmes.

There are limitations to our study: it is an uncontrolled retrospective study on a small number of outpatients that are not representative of the general demented population.

In conclusion, high level cognitive functioning and severe euphoria at pre-treatment evaluations are significant predictors of unresponsiveness to RO intervention. Future research is required to confirm these preliminary results and identify who will respond to long-term RO.

Key points

- There is some evidence that reality orientation has benefits on both cognition and behaviour in people with Alzheimer's disease.
- The clinical characteristics of patients who respond to reality orientation are poorly understood. Objective selection criteria for those suitable for reality orientation are not available.
- Our retrospective study shows that lower mini mental state evaluation performance at baseline and the absence of euphoria are significant predictor variables of responsiveness to a one-month formal reality orientation programme in outpatients with mild-to-moderate dementia.
- Further research is required to determine the clinical profile of Alzheimer's disease patients who may benefit from short and long-term reality orientation.

Acknowledgements

References

1. Spector A, Orrell M, Davies S, Woods B. Reality orientation for dementia. (Cochrane Review). In The Cochrane Library Issue 3. Oxford: Update software, 2001.

2. Drummond L, Kirchoff L, Scarbough DR. A practical guide to reality orientation: a treatment approach for confusion and disorientation. Gerontologist 1978; 8: 568–73.

3. Spector A, Orrell M, Davies S, Woods B. Reality orientation for dementia: a systematic review of the evidence of effectiveness from randomized controlled trials. Gerontologist 2000; 40: 206–12.

4. De Vreese LP, Fioravanti M, Belloi L et al. Memory rehabilitation in Alzheimer's disease: a review of progress. Int J Geriatr Psychiatry 2001; 16: 794–809.

5. American Psychiatric Association (APA) Practice guidelines. Workgroup on Alzheimer's disease and related disorders. In Rabins P, ed. Practice Guideline for the Treatment of Patients with Alzheimer's Disease and other Dementias. Am J Psychiatry 1997; S154.

6. McKhann G, Drachman D, Folstein M et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. Neurology 1994; 39: 939–44.

7. Folstein MF, Folstein SE, McHugh PR. 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975; 12: 189–98.

8. Zanetti O, Frisoni GB, De leo D *et al*. Reality orientation therapy in Alzheimer disease: useful or not? A controlled study. Alzheimer Dis Assoc Disord 1995; 9: 132–8.

9. Katz S, Downs TD, Cash HR, Grotz RC. The index of ADL: a standardised measure of biological and psychosocial function. J Am Med Assoc 1963; 9: 914–9.

10. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969; 9: 179–8.

11. Loewenstein DA, Bates CB. The Direct Assessment of Functional Status (DAFS). Manual for Administration and Scoring. Miami Beach, FL: Neuropsychological Laboratories. The Wien Center for Alzheimer's Disease and Memory Disorders, Mount Sinai Medical Center, 1992.

12. Zanetti O, Frisoni GB, Rozzini L *et al*. Validity of direct assessment of functional state as a tool for measuring Alzheimer's disease. Age Ageing 1998; 27: 615–22.

13. Yesavage JA, Brink TL, Rose TL *et al*. Development and validation of a geriatric depression screening scale: preliminary report. J Psychiatr Res 1983; 17: 37–49.

14. Cummings JL, Mega MS, Gray K *et al*. The neuropsychiatric inventory: comprehensive assessment of psychopathology in dementia. Neurology 1994; 44: 2308–14.

15. Binetti G, Padovani A, Magni E *et al*. Delusions and dementia: clinical and CT correlates. Acta Neurol Scand 1995; 91: 271–5.

16. Frisoni GB, Rozzini L, Gozzetti A *et al*. Behavioral syndromes in Alzheimer's disease: description and correlates. Dement Geriatr Cogn Disord 1999; 10: 130–8.

17. Norusis MJ. SPSS×Advanced Statistic Guide. New York: McGraw-Hill, 1985.

18. Leiter FL, Cummings JL. Pharmacological interventions in Alzheimer's disease. In Stuss DT, Winocur G, Robertson IH, eds. Cognitive Neurorehabilitation. Cambridge: Cambridge University Press, 1999; 153–69.

19. Mega MS, Masterman DM, O'Connor SM *et al*. The spectrum of behavioral responses to cholinesterase inhibitor therapy in Alzheimer disease. Arch Neurol 1999; 56: 1388–93.

20. Perry RJ, Hodges JK. Attention and executive deficits in Alzheimer's disease: a critical review. Brain 1999; 122: 383–404.

21. Elias JW, Treland JE. Executive function and cognitive rehabilitation. In Hill RD, Bäckman L, Stigsdotter Neely A, eds. Cognitive Rehabilitation in Old Age. New York: Oxford University Press, 2000; 159–73.

22. Binetti G, Magni E, Padovani A *et al*. Executive dysfunction in early Alzheimer's disease. J Neurol Neurosurg Psychiatry 1996; 60: 91–3.