

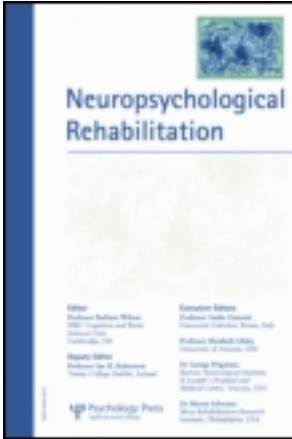
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A direct comparison of errorless and errorful therapy for object name relearning in Alzheimer's disease

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Developing rehabilitation techniques to combat cognitive decline is a key goal of healthcare strategies aimed at promoting increased longevity and better quality of life for individuals with Alzheimer's disease (AD). In AD, problems with episodic memory and word-finding greatly affect everyday life and, as such, these symptoms provide a clear clinical target for therapeutic interventions. Errorless learning (EL) has been proposed as a particularly effective technique for relearning in individuals with memory dysfunction, including AD. However, EL learning has rarely been directly contrasted with other more traditional trial-and-error techniques (errorful learning or EF) in individuals with AD, especially in the context of alleviating word-finding problems. In the current study, we directly contrasted the therapeutic gains of an EL learning paradigm (consisting of reading/repetition of object names) with an EF learning technique (comprised of phonemic/orthographic cueing) in eight mild to moderate AD patients with pronounced anomia. Both techniques were administered concurrently in

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sessions run twice a week over a five-week period. Therapeutic gains were assessed at one week and five weeks post-intervention using confrontation naming. Our results suggest that, both at the group and individual patient level, EL and EF techniques were equally effective. Correlational analyses of overall therapy gains and background assessments of patient neuropsychology revealed that individuals with better scores on measures of semantic memory, pre-intervention naming, and recognition memory demonstrated larger therapy gains. No individual patient showed a significant advantage for EL over EF learning, however, for patients that showed a numerical advantage in this direction. These results suggest that either EL or EF therapy can be used to alleviate word-finding problems in AD.

Keywords: Anomia; Alzheimer's disease; Errorless learning; Trial-and-error learning; Therapy; Memory rehabilitation; Anomia.

INTRODUCTION

Word-finding difficulties are a key and frustrating symptom of Alzheimer's disease (Lambon Ralph, Patterson, Graham, Dawson, & Hodges, 2003). Critically, word-finding problems directly impact on an individual's quality of life by making it more difficult to communicate with others (e.g., family and healthcare professionals) and manage daily affairs. Consequently, a role for speech and language therapists in the management, treatment and long-term care of patients with dementia is becoming more widely acknowledged and an increased rate of referrals for patients with neurodegenerative diseases is being made to speech and language therapy departments. A key problem facing healthcare professionals is deciding on the most effective form of therapy for name relearning in cases of neurodegenerative language impairment. Specifically, it is necessary to consider both the overall cognitive profile of the individual patient – i.e., their specific strengths and weaknesses – as well the demands made by the therapy on the family and support network who may be required to support relearning outside the clinic. In the current study we directly contrasted the benefits of two forms of therapy – errorless (EL) and errorful (EF) relearning techniques – in the same cohort of AD patients and explored which cognitive factors were associated with successful object name relearning.

Errorless learning originated from animal learning studies (Terrace, 1963) and is now widely studied by neuroscience researchers who are interested in brain plasticity (Buonomano & Merzenich, 1998; Tallal, Merzenich, Miller, & Jenkins, 1998). The basic premise behind EL learning is that standard learning/recovery may be limited by patients' errors because there might be reinforcement of the association between the stimulus and the erroneous

response due to a deficit in explicit declarative memory. By adjusting the intervention such that the patients are much less likely to make errors, better learning arises because the patients only reinforce the correct response. In Alzheimer's disease (AD) the most prominent cognitive impairment is an inability to learn and retain explicit episodic memories with relative preservation of implicit memory (Hodges, 2006; Lambon Ralph et al., 2003). However, individuals with AD frequently exhibit additional, albeit less marked problems in identifying and naming objects as well as concurrent difficulties with attention and executive functions (Hodges & Patterson, 1995; Perry & Hodges, 1999). Given this combination of deficits, EL learning may be particularly beneficial for re-acquiring previously known information in AD relative to more EF techniques because the patients' limited resources can be focused on a highly constrained learning experience.

Wilson and colleagues pioneered the use of EL learning for the treatment of memory impairment across a range of patients with acquired brain injury (Clare, Wilson, Breen, & Hodges, 1999; Wilson, Baddeley, Evans, & Shiel, 1994; Wilson & Evans, 1996). Broadly speaking, these studies can be split into two types: experimental and therapeutic. In the experimental studies, researchers have directly compared EL and EF learning. Most typically, studies have asked amnesic patients to learn arbitrary associations (i.e., paired associate learning and stem completion) and found that memory-impaired patients consistently do better if the learning paradigm prevents them from making EF responses (Baddeley & Wilson, 1994; Clare & Jones, 2008; Hunkin, Squires, & Tidy, 1998; Squires, Hunkin, & Parkin, 1997; Wilson et al., 1994). In the therapeutic studies, which have focused on the development or re-acquisition of practical everyday skills and knowledge, Clare and colleagues have extended these experimental findings to show that AD patients can learn to use memory aids and relearn the names of objects or people by the use of EL learning (Clare et al., 1999; 2000; Clare, Wilson, Carter, & Hodges, 2003; Clare, Wilson, Carter, Hodges, & Adams, 2001; Clare, Wilson, Carter Roth, & Hodges, 2002). For example, Clare et al. (2000) demonstrated that a small group of patients with AD could relearn the names of friends in their social settings through the use of EL learning. However, a key limitation with these earlier therapeutic studies is they only employed EL techniques so did not provide a direct contrast of the effects of EL and EF methods.

More recently, a limited number of studies have started to address this gap in the literature by directly contrasting the benefits of EL and EF methods in patients with dementia using within-subject comparisons (see below for a review of the earlier, larger-scale patient comparisons in stroke-related aphasia). In general, these studies have generated mixed results and have not consistently replicated the classic finding from experimental studies of amnesic patients (a clear advantage for EL over EF learning). While two of

the most recent studies in the literature have shown a clear advantage for EL over trial-and-error learning when acquiring novel and previously known face–name associations in AD (i.e., Haslam, Moss, & Hodder, 2010) or a novel procedural problem-solving task (Kessels & Olde Hensken, 2009), many other studies have not found this pattern. For instance, Dunn and Clare (2007) contrasted four learning techniques which varied in the degree to which they elicited errors during the learning of novel and previously known face–name associations. Critically, all of the conditions generated significant learning/relearning in their AD cohort but there was no significant difference in learning outcomes between those conditions that minimised errors relative to those that did not. Bier et al. (2008) explored learning of novel face–name associations in 15 patients with mild AD and obtained similar results. In their study, EL (immediate repetition) was contrasted with two error-reducing techniques (vanishing cues and spaced retrieval) as well as two trial-and-error techniques (varying with respect to whether the participants were given explicit or implicit task instructions). Bier et al. (2008) found that, although there was a significant difference between the amount of errors made in the learning phase across all five methods, this did not result in a significant advantage for EL over EF techniques; all five methods were equally effective. Similarly, Ruis and Kessels (2005) directly contrasted EL and EF therapy in a more severely impaired cohort of 10 AD patients who were learning face–name associations. Their results revealed an advantage for EL over EF learning after two consecutive learning trials. However, this difference disappeared at a subsequent delayed recall assessment, suggesting that the long-term benefits of EL and EF therapies were quantitatively similar. Metzler-Baddeley and Snowden (2005) demonstrated that their group of AD patients (four individuals) exhibited an advantage for EL over EF exposure when relearning face–name associations and object names. However, the EL greater than EF effect was only evident at the group level. At the individual patient level both EL and EF strategies were effective and no single patient showed a significant advantage for one technique over the other. More recently, Haslam, Gilroy, Black, and Beesley (2006) explored the acquisition of novel face–name–occupation associations in a cohort of AD and vascular dementia patients. The authors argued that EL learning might provide an advantage over EF learning only for the acquisition of highly specific information (i.e., face–name but not face–occupation associations). Although they found some evidence to support this position they also demonstrated that a number of their patients showed beneficial effects of both forms of therapy and many showed no evidence of an EL over EF advantage. In a more recent study (Haslam, Hodder, & Yates, 2011), there was no significant difference in learning novel face–name associations in trial-and-error vs. errorless learning procedures even though the patients attended equivalently to the stimuli in both conditions (as measured by a post-therapy familiarity recognition test).

Therefore, while the experimental studies of EL seem to show a consistent pattern of EL greater than EF in AD patients, there is a suggestion that EL may be equal to EF in the context of relearning. To date, however, the majority of these data has focused specifically on the acquisition of novel or previously known face–name associations or novel procedural tasks and has rarely explored the benefits of EL and EF methods for the reacquisition of previously known object names.

At this point, it is useful to consider the evidence from therapeutic relearning studies in cases of stroke-induced language impairment and anomia. Traditionally, object–name relearning studies in post-stroke populations have tended to employ techniques which are not completely error-free (Fillingham, Hodgson, Sage, & Lambon Ralph, 2003). For example, phonemic and orthographic cueing is commonly used to help and to improve naming accuracy of previously known verbal labels. Nonetheless, it tends to be the case that patients are encouraged to produce a response on every trial, frequently leading to the generation of erroneous responses. More recent studies have also started to employ EL techniques which explicitly aim – through task structure and the experimenter's instructions – to limit the likelihood of patients generating errors which may derail the relearning process. Therefore, the post-stroke relearning studies provide useful insights regarding the potential benefits of EL and EF therapies within the same group of patients in a therapeutic setting.

Fillingham and colleagues carried out a number of studies in post-stroke anomic patients using both EL and EF techniques which have shown that both types of therapy lead to similar, positive outcomes (Lambon Ralph & Fillingham, 2007). For instance, Fillingham, Sage, and Lambon Ralph (2006) directly contrasted an EL technique consisting of combined name repetition and reading in comparison with an EF method whereby patients were presented with progressively longer, dual phonemic and orthographic cues following an incorrect attempt at spontaneous (uncued) naming. Nine out of the 11 patients in this study showed significant relearning and of these 8/9 showed a pattern where EL was equal to EF. These studies were replicated, with variations of methodology (concurrent vs. serial delivery of therapy; provision of feedback: Fillingham, Sage, & Lambon Ralph, 2005a, 2005b). Likewise, very similar results have been found for relearning the names of actions even when the relearning method encouraged errorful production in the errorful condition (Conroy, Sage, & Lambon Ralph, 2009a, 2009b). As well as providing direct comparisons of EL and EF relearning of names, these studies are interesting because they explored the relationship between relearning efficacy and background aphasiological-neuropsychological status across the patients. In the most recent analysis which combined data across 35 patients, Lambon Ralph, Snell, Fillingham, Conroy, and Sage (2010) found that both the status of underlying executive-attentional skills

and the severity of the language (particularly phonological) impairment were significant independent predictors of relearning success.

Taken together the results from the review above suggest that EF and EL learning tend to be equally effective for relearning names in AD or stroke-related aphasia. These findings are in direct contrast with the original experimental studies of amnesic patients which showed a clear advantage for EL over EF therapy. In the current study we explored whether AD patients show the same pattern of EL equal to EF when they are asked to relearn the names of previously known and common everyday objects and animals (rather than specific names). In order to provide direct comparison across patient groups, we adopted the very same methodology as that used previously by Fillingham et al. and Conroy et al. in stroke-related aphasia. In addition, we investigated which neuropsychological factors are associated with overall improvement across therapies.

METHOD

Participants

Participants were selected on the basis of a clinical diagnosis of probable Alzheimer's dementia using the NINCDS-ADRDA consensus criteria (McKhann et al., 1984). Diagnoses were made by experienced healthcare professionals, specialising in old-age mental health, at memory clinics in either Bath (RWJ) or Manchester (ASB). A total of eight participants were included in the study. All had a prominent loss of declarative episodic memory characterised by both anterograde and retrograde memory difficulties, accompanied by impaired activities of daily living and impairment in at least one other area of cognition. As the focus of this study was on name relearning, patients were selected only if they had a profound anomia – as assessed by three established tests of picture naming (Table 1). All participants were native speakers of English and literate prior to the onset of dementia. This work was approved by local health authority ethics committees and informed consent was obtained for all participants.

Therapy method

In order to select items for both EF and EL therapy (and for the control sets), all participants had been asked to name, on three different occasions, a large battery of pictures. From each participant's battery, an item was selected only if it had been named on either 0/3 or 1/3 of these naming occasions. Items were divided into two therapy sets and a control set, and then matched for frequency (Baayen, Piepenbrock, & van Rijn, 1993), syllable length, number of phonemes and baseline naming ability. There were 20 items in each training set.

TABLE 1
Background neuropsychological assessment results for each participant

<i>Cognitive ability</i>	<i>Assessment</i>	<i>Max score</i>	<i>Cut off</i>	<i>MH</i>	<i>TA</i>	<i>LA</i>	<i>JP</i>	<i>JT</i>	<i>EM</i>	<i>DH</i>	<i>DP</i>
Naming	Boston Naming Test	60	42	16*	27*	16*	21*	23*	27*	31*	41*
	100-item naming test	100		69	54	54	89	75	70	76	72
	Graded Naming Test	30	12	5*	7*	5*	8*	3*	7*	5*	0*
Repetition	PALPA 8 non-word repetition	30	N/A	29	24	18	24	20	17	11	22
	PALPA 9 word repetition	80	78	77*	78	60*	–	78	70*	80	71*
Reading	PALPA 31	80	79	–	77*	70*	78*	80	78*	77*	79
Semantic memory	Pyramids and Palm Trees pictures	52	49	32	40*	32*	41*	48*	42*	48*	49
	Pyramids and Palm Trees words	52	49	33	49	39*	49	50	47*	49	46*
	64 Item Semantic Battery (WPM)	64	63	44	39*	41*	64	59*	42*	52*	44*
Episodic memory	Camden Recognition Memory Test for faces	25		13	11	16	7	15	21	16	19
	Camden Recognition Memory Test for words	25		12	10	17	7	16	18	16	8
Attention and executive function	Digit span forwards (max length)	14	5	6	5	5	2*	6	6	8	7
	Digit span backwards (max length)	14	2	3	2	2	2	3	2	4	3
	TEA	7	6	4*	8	7	7	6	6	7	–
	TEA/D	10	3	0*	7	0*	0*	4	3	2*	–
	WCST (categories completed)	6	1	–	6	0*	6	0*	6	1	–
Dementia severity	MMSE	30	26	21*	19*	9*	14*	23*	24*	16*	17*

PALPA = Psycholinguistic Assessments of Language Processing in Aphasia; TEA = Test of Everyday Attention (elevator counting subtest); TEA/D = Test of Everyday Attention with Distraction (elevator counting with distraction subtest); WCST = Wisconsin Card Sort Task. *Impaired performance.

For each group of selected items, we computed the pre-treatment naming accuracy as follows: any item which had been correctly named on one of the three baseline sessions was classified as correct and given a score of 1; if an item was not named on any of the three sessions it was scored as 0. This is a relatively conservative measure, given that it represents the very best performance level achieved by each participant prior to therapy. The intervention method was based on that used previously by Fillingham et al. (2005a; 2005b). In the EL therapy the picture was shown with the target word presented in spoken and written format, this was then repeated three times by the participant, and the next picture was then shown. The EF therapy method was based on picture naming with progressive phonemic and orthographic cues provided by the experimenter. Participants were first asked to name each item without a cue and if they were unable to produce the correct label they were provided with a sequence of progressively longer cues. The cueing procedure was stopped when the participant was able to produce the correct verbal label. If the target word was monosyllabic then the first phoneme and letter was initially given followed on the subsequent trial by the first two phonemes and letters of the word. If they were still incorrect then the whole word was given to repeat and/or read. If the word was multisyllabic, then the first phoneme and letter was given, then the first syllable (spoken and written) and finally the whole word in spoken and written form. If the whole word was provided via cueing then the participant was encouraged to repeat/read the target name. The next picture was then presented. Each item was presented three times per session for both the EF and EL therapy sets. There was a total of 10 sessions (participants were seen twice a week over a period of 5 weeks), each lasting between 40 and 60 minutes. Learning was assessed at 1 week and 5 weeks post-therapy; no maintenance or additional therapy took place during this assessment period. The control sets (i.e., the untreated items) were only seen at the week 1 and week 5 assessment points – i.e., when all interventions had been completed.

To test the reliability of our EL and EF learning techniques to minimise or induce errors during learning, we directly contrasted the percentage of errors made during therapy for each technique (collapsing across all 10 therapy sessions). Sixty five percent of initial responses were incorrect during EF therapy, compared to less than 1% in the EL condition, $t(7) = 14.8$, two-tailed $p < .001$.

Pre-treatment performance on language and cognitive assessment

A number of neuropsychological assessments were carried out prior to therapy to characterise the nature of the impairment in each patient. For all

assessments, performance was judged to be impaired if the score fell two standard deviations below the control mean or below the published cut-off score for the test.

Naming. Picture naming was assessed using three tasks: a 100-item naming test (Lambon Ralph, Moriarty, & Sage, 2002); the Boston Naming Test (BNT; Kaplan, Goodglass, & Weintraub, 1983); and the Graded Naming Test (GNT; Warrington, 1997). These assessments consist of black and white line drawings with a range of familiarity ratings (including both common and less common item names). These measures formed the basis of our assessment of anomia severity. All patient results (see Table 1) are ordered by their BNT scores.

Repetition. All participants completed the PALPA 8 non-word repetition task (Kay et al., 1992) which contains 30 non-words varying in syllable length from one to three syllables (e.g., kruft, duter, inima). Seven out of eight participants completed PALPA 9 word repetition which is broken down by imageability and frequency (Kay, Lesser, & Coltheart, 1992).

Reading. The PALPA 31 imageability by frequency reading test (Kay et al., 1992) was completed by all participants. This test contains 80 words of which 20 are highly imageable and high frequency, such as “church” and “letter”; 20 are highly imageable and low frequency, such as “axe” and “tractor”, 20 are low imageable and high frequency, such as “attitude” and “thought”, and 20 are low imageable and low frequency, such as “dogma” and “mercy”.

Episodic memory. The Camden Recognition Memory Test for faces and words (Warrington, 1996) was used to assess episodic memory in all patients.

Semantic memory. All 8 participants undertook both the picture and the word versions of the Pyramids and Palm Trees Test (Howard & Patterson, 1992). This test assesses semantic knowledge by requiring participants to match either one picture to another or one word to another (from a choice of two) on the basis of semantic association. For example, for a “pyramid”, the participant has to select either a “palm tree” or a “fir tree”. Comprehension was also assessed using the 64-item spoken word–picture matching task from the Cambridge Semantic Battery (Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000).

Attention and executive function. Seven out of eight participants were assessed on two auditory subtests of the Test of Everyday Attention (Robertson, Ward, Ridgeway, & Nimmo Smith, 1994). The first – Elevator Counting

without Distraction – assesses sustained attention. Participants hear a series of beeps at random time intervals (representing floors in a lift). They are asked to count the number of beeps (range 3–14) in order to track which floor the lift has arrived at. At the end of each trial participants are asked to report the number of tones they have heard. A table of written numbers was provided to enable responses from patients with number naming difficulties. Use of their own fingers to indicate the number of tones was also accepted. The second, more demanding, subtest – Elevator Counting with Distraction – assesses divided attention. Participants hear a series of high and low beeps. They are asked to count only the low beeps, while ignoring the high beeps. Beeps are presented in a random order at random time intervals (range 2–14).

In addition, participants were assessed with the Wisconsin Card Sort Task (WCST; Grant & Berg, 1993; Stuss et al., 2000). This test consists of 128 cards which each vary along three feature dimensions – i.e., colour (red, yellow, blue, green), shape (circle, triangle, square, cross) and number of symbols present on the card (one, two, three, four). Participants have four reference cards laid out in front of them and are asked to sort the remaining cards into four piles based on an unspecified sorting principle which they must deduce through trial and error (e.g., sort by colour, by form or by number). Participants are given feedback on whether their sorting technique is right or wrong. Once 10 consecutive cards have been placed correctly, the tester changes the sorting rule (e.g., sort by number, instead of the previously correct sort by form rule) without explicitly informing the participants of the rule change. We report the number of categories completed (maximum = 6) to provide an indication of how many rule changes the participants were able to detect.

RESULTS

Background neuropsychology

Table 1 summarises the pre-treatment neuropsychological test results. All eight participants showed impaired performance on the full range of picture naming tests. Three participants showed excellent repetition skills and two participants were within the normal cut-offs for word reading (PALPA 31). All patients showed some evidence of semantic difficulties, with seven out of eight patients showing impairment on at least two of the three receptive semantic tests. There was generally good performance on the sustained attention task of the TEA with six out of seven participants scoring within normal limits. The divided attention task from the TEA showed much greater variation in ability across the participants. The WCST also revealed a range of

cognitive skills across the participants, with most patients either doing well or failing the test completely.

Therapy results

Group analyses. The group level relearning data were assessed using a 3 (therapy condition: EL, EF, untreated) by 3 (time point: baseline, post-therapy 1 week, post-therapy 5 weeks) within subjects ANOVA. This analysis revealed main effects of both therapy, $F(2, 14) = 15.70, p < .001$, and time point, $F(2, 14) = 37.72, p < .001$, as well as a significant interaction between the two variables, $F(4, 28) = 5.75, p < .005$, see Figure 1. To break this result down further we first explored differences in naming accuracy across the three therapy conditions (EL, EF, untreated) at each time point (the baseline time point was excluded from this analysis as scores were matched before intervention). At week 1 post-intervention both EL and EF therapy produced better naming accuracy compared to no treatment, $t(7) = 5.1$, two-tailed $p = .001$; $t(7) = 5.3, p < .001$, respectively. However, overall gains did not differ across the two forms of intervention, $t(7) = 1$. A qualitatively similar pattern was observed at week 5; there was no difference between EL and EF therapy, $t(7) = 1.2, p > .2$, and both interventions produced significant gains compared to no treatment, $t(7) = 2.9, p = .021$; $t(7) = 4.5, p = .003$. We next looked at name relearning and retention over time for each therapy condition separately. For EL therapy, naming was significantly better at week 1 and week 5 post-therapy compared to baseline, $t(7) = 6.3, p < .001$; $t(7) = 4.0$,

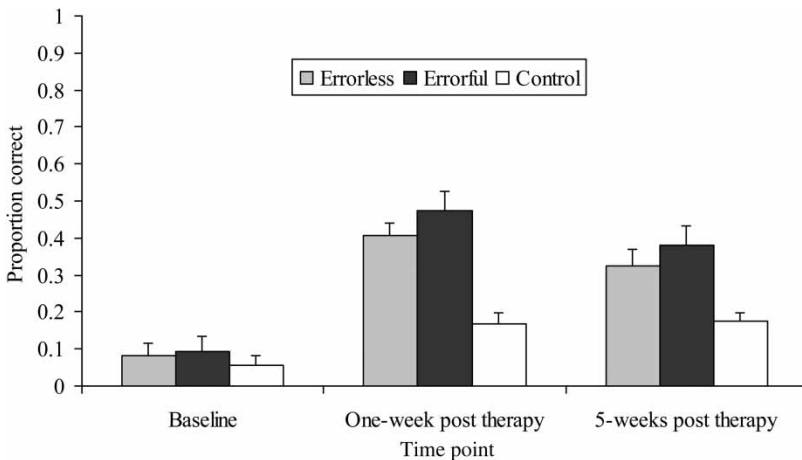


Figure 1. Group level effects of errorless and errorful therapies on name relearning. Error bars represent the standard error of the mean.

$p = .005$; however, performance declined slightly between the two post-therapy assessments, $t(7) = 3.2$, $p = .014$. In the EF condition, naming improved significantly at week 1 and week 5 post-therapy, $t(7) = 5.4$, $p < .001$; $t(7) = 4.8$, $p = .002$, and there was no decline in performance between the two post-therapy assessments. Exploration of naming performance in the untreated condition revealed a mild degree of improvement relative to baseline at post-study assessments in week 1, $t(7) = 3.3$, $p = .013$, and week 5, $t(7) = 6.5$, $p < .001$, with no decline in performance between week 1 and 5, $t(7) = 1$.

Single case analyses (Figure 2). In the EL condition two participants (DH and DP) showed improvement relative to baseline at week 1 and week 5 post-therapy (McNemar two-tailed exact, $p = .01$ to $< .001$). Two additional participants (JP and MH) showed an improvement relative to baseline at week 5 (McNemar two-tailed exact $p = .04$ and $.03$, respectively) and a borderline significant improvement at week 1 (McNemar two-tailed exact $p = .07$). JT showed a therapy effect at week 1 only (McNemar two-tailed exact $p = .03$). TA, LA and EM showed no significant benefits of EL therapy (McNemar two-tailed exact $p > .1$).

In the EF condition three participants (DH, LA and JP) showed a significant therapy effect at both week 1 and week 5 (McNemar two-tailed exact $p = .02$ to $< .001$). Three additional participants (JT DP, and EM) showed an effect of therapy at week 1 (McNemar two-tailed exact $p = .03$ to $< .001$) and two of these participants (DP and EM) showed a borderline effect at week 5 (McNemar two-tailed exact $p = .06$). EM showed a significant decline between week 1 and week 5 follow-ups (McNemar two-tailed exact $p = 0.01$). TA and MH showed no significant benefits of EF therapy (McNemar two-tailed exact $p > .1$).

To assess whether individual patients showed better performance with either EL or EF learning at each of the post-therapy assessments chi-square comparisons were carried out for each patient. EM performed significantly better in the EF condition at 1 week post-therapy ($\chi^2 = 7.7$, two-tailed $p = .005$), however this difference did not reach significance at the week 5 assessment ($\chi^2 = 1.8$, two-tailed $p = .17$). Interestingly, EM achieved the best scores on background assessments of recognition memory, but was also the least severe patient in our cohort as judged by the MMSE. The remaining patients showed no difference between EL and EF therapy at either week 1 ($\chi^2 < 1.5$) or week 5 post-therapy ($\chi^2 < 1.5$).

The results from the single case analyses align perfectly with the group-level data by suggesting that both EL and EF therapy are just as effective for name relearning in patients with AD.

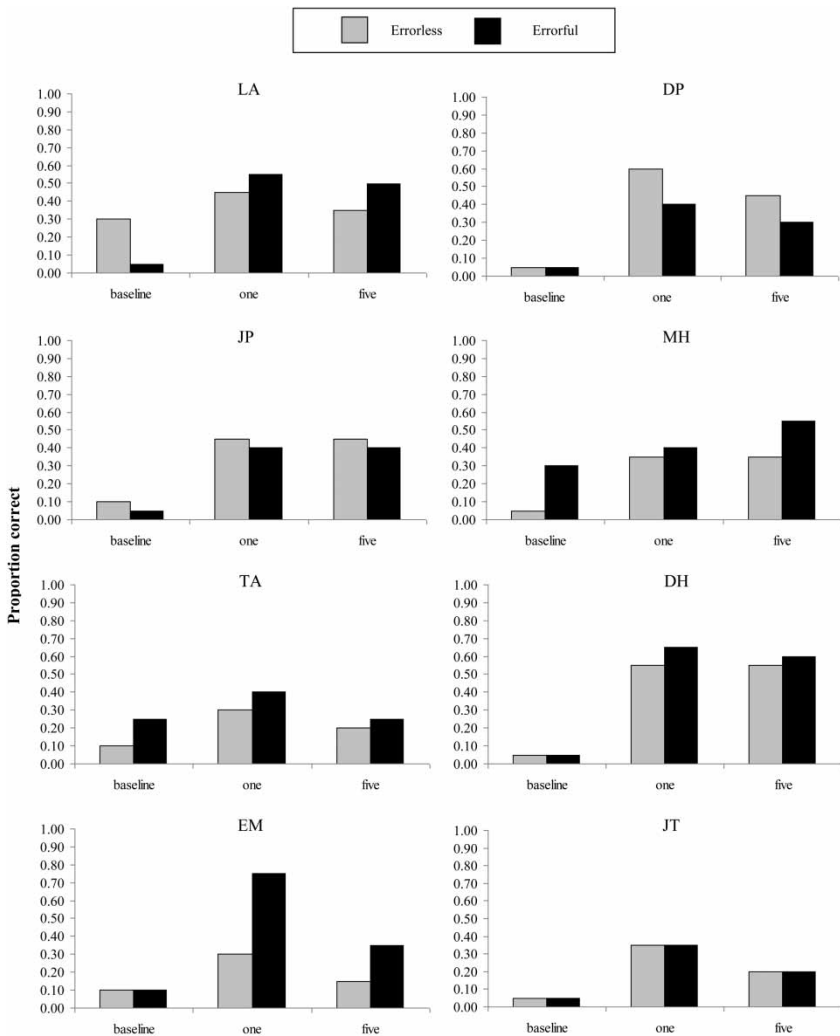


Figure 2. Effects of errorless and errorful therapies on individual patient relearning.

Correlations between therapy gains and neuropsychological factors. Given the limited number of participants, we conducted a final purely exploratory analysis of the relationship between background assessments of cognitive status and therapy gains in our AD cohort using correlational techniques. Three comparisons were made: (1) we assessed which background neuropsychological assessments correlate with the size of the immediate therapy effect (the difference in scores at baseline and week 1 post-therapy); (2) which

correlate with the long-term effect (baseline vs. week 5 accuracies); and (3) which correlate with the difference between EL and EF therapy outcomes.

At week 1 post-therapy, overall relearning was positively correlated with the picture version of the Pyramids and Palm Trees Test ($r = .81, p = .01$ two-tailed), an assessment of associative semantic knowledge. In addition, a number of other correlations approached significance (i.e., $p < .1$). Performance on two of the three background picture naming tests (the Boston Naming Test and the 100-item naming test) were positively associated with name relearning ($r = .67, p = .071$; $r = .67, p = .066$, respectively), as was forward digit span ($r = .69, p = .057$) and the Camden Recognition Memory for Faces Test ($r = .62, p = .09$). At week 5 post-therapy, there were borderline significant correlations between overall relearning scores and the 100-item naming test ($r = .68, p = .062$), the 64-item word-picture matching task ($r = .65, p = .076$) and Elevator Counting with Distraction from the Test of Everyday Attention ($r = -.7, p = .077$). Only one background test correlated with the difference between EL and EF learning in our AD cohort. Poor performance on the Camden Recognition Memory Test for Words was associated with an advantage for EL over EF conditions at week 1 ($r = -.74, p = .033$) and week 5 post-therapy ($r = -.71, p = .046$).

DISCUSSION

Anomia is a commonly recognised feature of Alzheimer's disease (AD) that typically follows the initial period of amnesia and leads to increasing difficulties with communication and activities of daily living as the disorder progresses (Lambon Ralph et al., 2003). A number of potential strategies have been proposed to facilitate relearning in cases of acquired memory and/or language dysfunction. Errorless learning (EL) has been suggested to be a particularly useful technique for patients with amnesia because it does not require the recipient to monitor and filter out errors which could potentially derail the relearning process (Clare & Jones, 2008). In contrast, speech and language therapy for patients with anomia after stroke has shown that trial-and-error techniques such as phonemic and orthographic cueing (referred to here as errorful learning or EF) can be equally beneficial when re-acquiring verbal labels (Lambon Ralph & Fillingham, 2007). The aim of this study was to contrast both of these techniques for the first time in a case-series of AD patients in the context of a therapeutic relearning study targeting the re-acquisition of previously known object names (not just specific names as per the current AD literature). In addition, we explored which characteristics of patients' neuropsychological profiles were associated with overall therapeutic gains. The main findings from this study can be summarised in the following points:

1. There was no evidence for a selective benefit of EL over EF learning. At the group level EL and EF learning techniques were equally beneficial for the recovery of object names in our AD cohort. Relative to untreated control items both forms of therapeutic intervention lead to significantly improved naming at one week and five weeks post-intervention.
2. Individual patients varied considerably in the extent to which they demonstrated relearning. A number of patients benefited from both EL and EF therapies. However, no individual patient showed an advantage for EL over EF therapy. In contrast, one patient performed better on EF relative to EL learning (i.e., patient EM).
3. A number of neuropsychological factors correlated with the overall magnitude of recovery observed in our cohort. Semantic memory status, pre-intervention naming ability and recognition memory status all positively correlated with the magnitude of improvement in naming abilities post-therapy. In contrast, only recognition memory status correlated with the difference score of EL minus EF learning, suggesting that patients who showed a numerical advantage for learning in the EL condition were more likely to have poorer recognition memory.

The use of EL techniques in human participants originated from a number of experimental studies which looked at learning in amnesic patients (Baddeley & Wilson, 1994; Squires et al., 1997; Wilson et al., 1994). In these investigations it was shown that individuals were considerably better at learning novel information – typically in the context of stem-completion or paired associated learning tasks – if they were not allowed to make errors. In contrast, overall learning was considerably poorer when patients were allowed to generate incorrect responses, or when the learning environment was structured such that errors were inescapable. It has been argued that this selective advantage for EL over EF learning arises from the nature of the memory impairment in amnesic patients which specifically disrupts explicit declarative memory leading to an over-reliance on implicit memory (Baddeley & Wilson, 1994). In AD the most prominent cognitive impairment is an inability to learn and retain explicit episodic memories with relative preservation of implicit memory (Hodges, 2006; Lambon Ralph et al., 2003). Therefore, within this group of patients we might have expected to see a consistent advantage for EL over EF therapy conditions. In contrast, we found that both forms of therapy were equally effective. There are a number of reasons why this pattern of results may have been found. Firstly, the classic experimental studies of learning in amnesic patients used very different tasks (stem-completion and pair-associate learning of arbitrary word lists) to those employed in the current study (picture naming). Moreover, no attempt was made in the current study to deliberately induce errors during

therapy; instead, they occurred naturally as a result of our phonemic/orthographic cueing procedure. Secondly, our study focused on the re-acquisition of previously known object names rather than learning novel/arbitrary associations. Residual knowledge regarding the identity of the therapy items may have been used to constrain information processing and to help filter out potential errors leading to better than expected performance in the EF condition. Indeed, the results of our correlational analyses support this interpretation by showing that patients who demonstrated the greatest degree of therapeutic gains tended to have better overall semantic abilities, i.e., better performance on the Pyramids and Palm Tree tests and word-picture matching.

Previous therapeutic studies in AD have found EL to be an effective technique for learning or recovering previously known information (Clare & Jones, 2008). However, in a number of these studies EL learning was not directly contrasted with other more EF techniques such as trial-and-error learning (Clare et al., 1999, 2000, 2001, 2002, 2003). Therefore, it is unclear whether the patients in these studies would have shown a similar level of improvement with EF methods, as was the case with the patients in our current investigation. A collection of more recent studies have directly compared EL and EF techniques in the context of relearning specific face-name associations. Interestingly, the results of these studies have shown that EL and EF therapies often result in a similar degree of learning/recovery. For instance, Dunn and Clare (2007) contrasted four different intervention techniques in a cohort of patients with AD. Each of these techniques varied considerably in the extent to which they induced errors in the learning phase of the study. Interestingly, all four conditions facilitated learning/recovery, but rate of errors did not modulate the effectiveness of therapy. Similarly, Bier et al. (2008) contrasted five different forms of therapy, which elicited varying degrees of errors in the learning phase (i.e., one EL technique, two error-reducing methods and two trial-and-error interventions), in a cohort of 15 mild AD patients. All five methods produced a similar degree of learning. A similar pattern of results has been found by a number of other studies which have assessed AD patients across a range of different severity stages using direct comparisons of EL and EF therapy methods (Haslam et al., 2006; Metzler-Baddeley & Snowden, 2005; Ruis & Kessels, 2005). Our findings extend this body of work by demonstrating the same pattern holds for the relearning of object names in patients with mild/moderate AD. Moreover, our results reinforce the point that the presence of amnesia in AD should not preclude the use of EF therapy techniques, which can be just as effective as EL methods.

Comparisons of EL and EF therapy for object name relearning in post-stroke aphasic patients have also suggested that both forms of therapy lead to a similar degree of recovery (Fillingham et al., 2003; Lambon Ralph &

Fillingham, 2007). Moreover, these studies have suggested that the degree of executive attention impairments in addition to language status play an important role in predicting the extent to which patients benefit from therapy (Lambon Ralph et al., 2010). In the current investigation, which used almost identical methods, we found that overall learning in AD was correlated with the integrity of semantic knowledge and language abilities; patients with better verbal/nonverbal comprehension skills and less severe anomia were most likely to benefit from therapy. AD patients were also more likely to show recovery in naming if they had good recognition memory skills, although the correlation between these two factors was weaker. The only neuropsychological factor which correlated with the difference between EL and EF learning at post-therapy assessment was recognition memory status; individuals who showed a numerical advantage in favour of EL learning tended to have poor recognition memory scores whereas those who showed an advantage for EF learning tended to have higher scores on the recognition memory tests. In line with this finding, patient EM who had the highest score on assessments of recognition memory was the only patient to show an EF over EL advantage. However, it is important to consider these results in the light of the finding that most patients showed improvement in both the EL and EF therapy conditions.

The results of this study have practical implications for choosing appropriate clinical intervention strategies to target name relearning in AD patients. The application of EL learning has been proposed as a particularly useful technique for patients with amnesic memory problems (Baddeley & Wilson, 1994; Clare & Jones, 2008). In the current study we have shown that trial-and-error techniques can produce equivalent results even in the context of profound memory problems. Therefore, it would seem that both techniques are of potential value. Nonetheless, there are a number of practical considerations which need to be taken into account when deciding whether to favour either EL or EF interventions for a given patient. During the administration of the therapy sessions it became clear that many of the patients found the EF technique more effortful and engaging than EL therapy (see also Conroy et al., 2009b). This was particularly noticeable for the less severe patients and may well have practical implications for the maintenance of therapy outside the clinic (milder patients may be less likely to engage in maintenance of therapy outcomes if they find that the materials do not stimulate them). In contrast, the more severe patients provided more positive feedback for the EL therapy conditions; both patients and spouses noted that these techniques would be easier to practise and maintain in a home environment. Therefore, it is important to consider both the severity of the individual patient and the potential for maintaining therapy in a home environment post-clinical intervention, when deciding on whether individuals should be given EL or EF relearning interventions.

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