Learning capacity in early-stage Alzheimer's disease: The role of feedback during learning on memory performance

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Abstract
Alzheimer's disease is characterized by a decline in episodic memory and executive functioning, hampering learning ability. Insight into outcome-based learning capacity may be relevant for optimizing the learning potential of these patients. To date, mixed results have been found in studies in which cognitively impaired participants have to learn based on positive and negative outcomes. In this study, we investigated the role of negative and positive feedback on memory performance and participants' ability to adjust their behaviour accordingly in a sample of 23 early-stage AD patients and 23 matched healthy controls. We administered a novel computerized object-location memory task, in which participants were instructed to learn and memorize the locations of different everyday objects following errorless learning (EL) and trial-and-error learning (TEL). A separate probabilistic TEL task was employed in which participants had to learn how to adjust their behaviour accordingly. Error frequency during acquisition of object locations was unrelated to later recall performance. Although the error monitoring system seems intact in patients with early-stage AD, errors during learning are likely acting as a source of interference causing difficulty in storage or retrieval of object locations.
INTRODUCTION

Alzheimer’s disease (AD), the most common cause of dementia, is marked by an irreversible decline in cognitive functions hampering everyday functioning. In the early stages of the disease progression, cognitive impairments are present, while functional decline is either absent or minimally present (i.e. referred to as mild cognitive impairment or MCI; Albert et al., 2011) or mild (i.e. referred to as mild dementia; McKhann et al., 2011; Sperling et al., 2011). Patients with early-stage AD are at greater risk of experiencing gradual cognitive decline, not only in episodic memory, but also in executive functioning (EF; Alves et al., 2021; Bastin & Salmon, 2014; El Haj, 2016; Gauthier et al., 2006). Both episodic memory and EF are particularly important for acquiring new information, monitoring one’s performance and effectively adapting one’s behaviour following changes in contingencies in the environment (e.g. Cristofori et al., 2019; Dickerson & Eichenbaum, 2010; Grober & Kawas, 1997). The cognitive impairments present in early-stage AD can thus be expected to interfere with the patients’ capacity to learn and adapt optimally. While memory (dys)function has been extensively studied in both MCI and AD patients, declarative learning has been scarcely examined in these patients (see, e.g. de Wit et al., 2023). Moreover, the underlying cognitive mechanisms of impairments in learning and adaptation are largely unclear, making it difficult to develop interventions that may help to improve learning capacity and memory performance in patients with early-stage AD.

Prior research has suggested that using approaches relying on errorless learning (EL) may be an effective method to improve learning outcomes in patients with early-stage AD. During EL, new information of skills is acquired through observation or strict instructions where the occurrence of negative outcomes (i.e. errors, negative feedback) is prevented as much as possible. This form of learning reduces interference of erroneous responses and results in a more accurate recall of information (Terrace, 1963). Beneficial effects of EL have been observed not only in patients with early-stage AD (Callahan & Anderson, 2019; Roberts et al., 2018), but also in neuropsychiatric disorders (Kern et al., 2003; Pitel et al., 2010) and in cognitively unimpaired older adults (e.g. Guild & Anderson, 2012). However, other studies in early-stage AD patients have reported beneficial effects of trial-and-error learning (TEL), during which participants have to learn and adapt their behaviour based on positive and negative outcomes (see, e.g. de Werd et al., 2013; Kerkhof et al., 2021). TEL differs fundamentally from EL in that the former assumes that the individual learns through perceived associations between events and subsequent negative outcomes, whereas negative outcomes are absent during EL (see, e.g. Cyr & Anderson, 2018; Ownsworth, 2018). The mechanistic underpinnings of TEL have been studied for many decades (Maia & Frank, 2011; Shteingart & Loewenstein, 2014), while much less is known about the underlying mechanisms of EL.

The latest EL theory proposes a prominent role for executive function, in particular error monitoring, facilitating the EL advantage (Clare & Jones, 2008). According to this principle, erroneous responses made during learning will also be activated during retrieval along with the correct response, as both type of responses are encoded in the same neural activity pattern. Executive processes are crucial for detecting and monitoring correct and incorrect responses and allow us to adapt our behaviour based on observed outcomes (i.e. feedback; Alexander & Brown, 2010; Luu et al., 2009), so that the information will be correctly stored in memory. Poor error monitoring can lead to errors not being recognized as incorrect responses, causing them to be incorrectly stored in memory (Bertens & Brazil, 2018). Several studies found a reduced ability to detect and correct errors in patients diagnosed with neurodegenerative diseases (e.g. AD) and acquired brain injury compared to healthy controls (Bertens et al., 2015; Bettcher et al., 2008; Bettcher & Giovannetti, 2009; Ito
& Kitagawa, 2005; Wong et al., 2019). In addition to incorrectly storing information, poor performance can also be due to deficits in updating expectations and modifying behaviour based on positive and negative outcomes. Adapting behaviour based on feedback requires cognitive flexibility and, in particular, the ability to learn from positive and negative outcome, estimate the likelihood or prior probability that reversals can occur and an understanding of task (Izquierdo et al., 2017). That is, to select an appropriate action, reversal learning is needed as reversal learning emphasized the need to withhold the previous rewarding responses when this behaviour is no longer rewarding and adjust one’s response to that most likely leads to positive feedback. For instance, Shohamy et al. (2008) used a probabilistic reversal learning task and showed that patients with amnesia due to hypoxic brain injury were unable to reverse their responses when stimulus–outcome contingencies changed and continued to respond to the stimuli with the same response they learned in the acquisition phase. On the other hand, patients diagnosed with Parkinson disease were prone to learn a new stimulus–response association during the reversal by selecting a new cue and predict the outcome. Still, the impact of reinforcers on the cognitive mechanisms through which the beneficial effects of EL or TEL emerge remains poorly understood.

The aim of this study was to examine learning capacity during EL, TEL and probabilistic TEL in patients with early-stage AD and memory deficits. Our goal was to contrast learning exclusively from positive feedback (EL), learning from both positive and negative feedback (TEL) and the capacity to use feedback to adapt behaviour accordingly on a trial-by-trial basis. We employed a novel spatial learning task, that is, the ‘Drawer task’ (Scheper et al., 2019, 2021, 2023), in which the frequency of errors (defined as incorrect responses) committed during the acquisition phase of EL (i.e. 0 incorrect responses) and TEL (i.e. 1, 2, 3, 4 or 5 incorrect responses) was predetermined. This enabled us to examine the impact of positive and negative outcome during learning on later memory performance. Compared to traditional EL tasks, that is, word-stem learning task, we employed a more ecologically valid task by appealing to visuospatial learning in which patients had to search for objects at different locations and remember their locations (e.g. where have I stored my glasses?). Moreover, we employed a probabilistic associative reversal learning task (Iglesias et al., 2013) to explore whether patients with early-stage AD are able to modify their behaviour based on probabilistic TEL. Based on previous studies (Scheper et al., 2019, 2021, 2023), we hypothesized an EL advantage compared to TEL in both patients with early-stage AD and matched cognitively unimpaired controls. In early-stage AD patients, we expected a worse memory performance after TEL compared to healthy controls, because the larger amounts of errors during learning compared to EL puts a greater burden on the already impaired object-location memory system (Poos et al., 2021). Next, we hypothesized that early-stage AD patients would perform worse on the probabilistic TEL task because of poorer ability to detect and adapt behaviour based on positive and negative outcomes in which the contingencies are probabilistic relative to healthy controls. The latter should be reflected in a worse general task performance, that is, a higher proportion of incorrect responses (Bettcher & Giovannetti, 2009; Levy-Gigi et al., 2011; Pezzetta et al., 2022). Moreover, Levy-Gigi et al. (2011) argued that the deficit in adapting behaviour was not influenced by positive or negative feedback in patients with amnestic MCI. Yet, Wessa et al. (2016) found that patients with amnestic MCI were able to learn from negative outcomes, but not from positive feedback. Hence, these conflicting findings make it difficult to formulate specific hypotheses on the effect of feedback processing on the ability to adapt behaviour accordingly. That is, it is unclear whether early-stage AD patients are more or less likely to stay with their response after positive feedback, referred as ‘Win-Stay’ (WS), and/or to shift from their last response after negative feedback, known as ‘Lose-Shift’ (LS). Overall, impairments in learning from probabilistic outcomes should be reflected by lower proportions of WS and LS tendencies compared to healthy controls. Ergo, this conflicting pattern of evidence emphasizes the importance of systematically exploring the role of positive and negative outcomes during learning on performance.
METHODS

Participants

For the comparison of the EL and TEL performances using a mixed design, a minimum sample size of 14 per group was required according to the power calculations, presuming a medium effect size ($r = .30$), a power of (1-\( \beta \)) .85 and a correlation among repeated measurements of .50 (G*Power; Erdfelder et al., 1996). In this study, early-stage AD patients were selected based on the Clinical Dementia Rating scale (CDR; Hughes et al., 1982; Morris, 1993), which was administered by geriatricians working at the recruiting hospitals. Early-stage AD was defined as a CDR score of .5 or 1, indicating MCI or mild dementia respectively. We recruited 23 patients with early-stage AD (15 with MCI and 8 with mild dementia) and 23 healthy controls, group-matched for age, sex and intelligence using the National Adult Reading Test (Schmand et al., 1992). All participants had Dutch as their native tongue. Recruitment of patients took place at Radboud University Medical Center and Canisius Wilhelmina Hospital in Nijmegen, The Netherlands. Healthy controls were recruited through various social networks. Cognitive impairments, episodic memory and executive functions were assessed in all participants using the Dutch version of the Montreal Cognitive Assessment (Kessels et al., 2022; Nasreddine et al., 2005), the Doors Test (Baddeley et al., 1994) and the Trail Making Test B/A (Bowie & Harvey, 2006; see Table 1 for demographic characteristics of the participants) respectively. The study was conducted in accordance with the Declaration of Helsinki. All participants participated on voluntary basis, gave written informed consent and received a small financial compensation for their participation. This study received ethical approval from the research ethics committee.

Materials

Drawer task

The Drawer task was used to measure memory performance for object locations (Scheper et al., 2019). This is a computerized learning task that consists of an acquisition phase immediately followed by a recall phase. The acquisition phase includes an EL and a TEL condition, which makes it possible to study the impact of negative outcomes on memory consolidation. Participants were shown 25 drawers in a

<table>
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<td><strong>Early-stage AD patients (N=23)</strong></td>
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<td>Sex M/F</td>
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Abbreviations: AD, Alzheimer's disease; MIS, Memory Index Score; MoCA, Montreal Cognitive Assessment; NART, National Adult Reading Test; TMT, Trail Making Test.
5 × 5 layout and, depending on the task condition, had to either store or find each of 20 different everyday objects (e.g. a football, a pencil) by clicking with the mouse on the drawers. They were instructed to memorize the correct location of the object after selecting the correct drawer (i.e. the drawer in which the object was ‘hidden’). The 20 objects were subsequently presented at the bottom of the screen and no time limit was given (see Figure 1 for example of a sample trial per condition of the drawer task). The instruction between the EL and TEL condition only differed with respect to the placement of the objects. All other instructions were identical (see also Appendices A and B for written instruction of the EL and TEL condition respectively). Participants always started with the EL condition followed by the recall phase to prevent intervention of errors made during TEL with the EL condition.

In the EL condition, participants were asked to randomly place the 20 objects in one of the available drawers. The correct drawer was defined by every first allocation of each object. In other words, no errors could occur during the acquisition. Hence, selecting a drawer was followed by a blue square and

![Figure 1](https://bpspsychub.onlinelibrary.wiley.com/doi/10.1111/jnp.12330)
a lock. The lock served the purpose of indicating that none of the remaining objects could be placed in the drawer. Participants were asked to remember its location for the recall phase.

In the TEL condition, participants were instructed to find the 20 objects in one of the available drawers. They had to memorize the correct drawer after finding out in which drawer the object was stored. Erroneously selected drawers were indicated by a red square and the correct drawer by a blue square. The number of different drawers that had to be selected (i.e. the number of ‘clicks’) before the correct drawer was ‘found’ was preset and unknown to the participants. That is, participants had to select 1, 2, 3, 4 or 5 unique ‘incorrect’ drawers before they found the drawer in which the object was stored. The error frequency manipulation consisted of four trials and was presented in a randomized order to hamper the participants’ anticipation of the number of incorrectly selected drawers.

A free recall phase immediately followed the acquisition phase of each condition. The same 5 × 5 chest of drawers (without locks) was presented. Participants were instructed to place each presented object in the drawer in which the object was found or stored during the EL or TEL acquisition phase. The objects were presented sequentially in a pseudo-random manner. Participants had just one attempt to store the object in its correct location and no feedback about its accuracy was given. Their performance was quantified by the mean absolute distance (in arbitrary units) between the selected drawer and correct drawer across all 20 objects, referred to as the ‘distance score’ (for more details about the measurement see Scheper et al., 2019).

A probabilistic associative reversal learning task was used to measure the ability to adjust behaviour based on positive and negative feedback (Iglesias et al., 2013; see Figure 2). Two abstract visual stimuli, a yellow or a green picture, were simultaneously shown. Participants had to learn through TEL which of the abstract visual stimuli was most often rewarded by pressing a button (right or left index finger) as quickly as possible. Feedback was provided about the accuracy of each

![Figure 2](https://bpspsychub.onlinelibrary.wiley.com/doi/10.1111/jnp.12330)
response by either a positive financial outcome (a one-euro coin) or negative financial outcome (a one-euro coin with a cross). Positive and negative feedback was given on 80% and 20% of the trials, respectively, for one stimulus. The stimulus most likely to lead to positive feedback switched multiple times across the six blocks of the task. In blocks 1, 3 and 5 the green abstract visual stimulus was considered to be rewarding (i.e. the green stimulus was followed by positive feedback in 80% of the trials) and in blocks 2, 4 and 6 the yellow stimulus was considered to be rewarding (i.e. the green stimulus was followed by positive feedback in 20% of the trials). Each block consisted of a different number of trials, respectively 40, 15, 25, 15, 25 and 40 trials, which resulted in a total of 160 trials. Participants were explicitly informed about the response reversals, but not when the reversals took place. Also, participants were instructed that the coins were not linked to the monetary reimbursement of the study.

Performances on the probabilistic TEL task was measured by three outcome measures. The first measure was the proportion of errors made during the reversal learning task. Here, only errors made after successful responses were taken into account. Next, the ability to adapt behaviour was measured based on the acquisition of the contingencies between stimuli and reward and on the principle to maintain successful behaviour after reward and switching after failure. When a participant selected the same stimulus as on the previous trial followed by positive feedback, this was defined as a WS response. The proportion of WS was calculated by dividing the number of WS trials by the number of trials in which positive feedback was given. The third measure was based on the LS responses, which was defined as the number of trials in which the participants selected the other stimulus after negative feedback. By dividing the number of LS trials by the number of trials in which negative feedback was provided, the proportion of LS was calculated. Only responses given within the time limit of 1500 ms were included.

**Data analysis**

To examine whether patients with early-stage AD and matched controls benefited from EL compared to TEL, a repeated measures general linear model (GLM) analysis was conducted with Group (patients with early-stage AD vs. controls) as between-subject factor, Learning condition (EL vs. TEL) as within-subject factor and distance score as dependent variable.

Second, to address the role of error frequency during the acquisition phase on subsequent recall, a repeated measures GLM analysis was performed for the TEL condition only with Group (early-stage AD patients vs. controls) as between-subject factor, Error frequency (performance on the 1, 2, 3, 4 and 5-error trials) as within-subject factor and distance score as dependent variables.

Next, to measure the proportion of errors on the reversal learning task, only the errors made after successful responses were taken into account and missing data were not analysed. The proportion of errors was calculated per block by dividing the total number of errors per block by the total number of trials to which a participant had given a response per block. Subsequently, a repeated measured GLM analysis was conducted with Group (early-stage AD patients vs. controls) as between-subject factor, Phase (blocks 1, 2, 3, 4, 5 and 6) as within-subject factor and proportion of errors as dependent variable to examine the ability to adapt behaviour per block and gain insight into reversal learning over time. Although most reversal learning studies cluster blocks in the acquisition condition (e.g. blocks 1, 3 and 5 taken together) and the reversal learning condition (e.g. blocks 2, 4 and 6 taken together; see, for instance, Budhani et al., 2006; Dillien et al., 2019), respectively, we sought to investigate the progression of whether participants adapted their behaviour over time by analysing the ability to adapt their behaviour per block. To examine whether patients with early-stage AD used different heuristic strategies after feedback (i.e. WS or LS) than controls, two GLM analyses were performed with Group (early-stage AD patients vs. controls) as between-subject factor and the proportion of WS and LS as dependent variables respectively. These two analyses of the probabilistic TEL addressed the question whether patients with early-stage AD differ in the tendencies to adapt their behaviour over time (i.e. per block) and based on positive or negative feedback (i.e. WS and LS) relative to healthy controls.
In addition, we examined the relationship between performance after EL and TEL and relationship between heuristic strategies, executive functions and memory per group using Spearman's rank correlation due to the small sample size.

RESULTS

Figure 3a shows the results of the performance of both groups on the Drawer task (distance score). Due to technical failure, data of one patient with early-stage AD were missing on the Drawer Task. Overall, the overall EL performance was superior to TEL across both groups ($F(1, 43) = 69.4, p < .001, \eta^2_p = .617$). Patients with early-stage AD performed overall worse on the subsequent memory recall than

![Graphs showing results of performance](https://bpspsychub.onlinelibrary.wiley.com/doi/10.1111/jnp.12330)
controls after both EL and TEL condition ($F(1, 43) = 16.1, p < .001, \eta^2_p = .272$). No interaction between Group and Learning condition was found ($F(1, 43) = .371, p = .546, \eta^2_p = .009$), indicating that even though patients with early-stage AD placed the objects further away from the correct drawer during the recall phase, they benefited as much as controls from EL compared to TEL.

In addition, the repeated measures GLM analysis on the role of error frequency during the acquisition phase of TEL on later recall, demonstrated that the performance of patients with early-stage AD was worse compared to controls ($F(1, 43) = 11.9, p = .001, \eta^2_p = .216$), see Figure 3b. However, no significant effect was found of the amount of erroneous attempts on the absolute distance in the recall phase (Error frequency: $F(3.64, 172) = .411, p = .782, \eta^2_p = .009$; Group × Error frequency: $F(3.64, 172) = 1.40, p = .240, \eta^2_p = .031$), meaning that after the occurrence of the first error during learning, making a second, third, fourth or fifth error did not have an additional adverse effect on the later recall performances.

During the probabilistic associative reversal learning task, data of three patients with early-stage AD were missing due to technical failure. Patients with early-stage AD significantly more often did not respond or responded after the time limit than the control group ($p = .018, \eta^2_p = .130; 8.6% of the trials in AD patients; 3.1% of the trials in controls; 5.8% of the trials for both groups taken together). There were no participants who did not make any correct response.

Figure 3c shows the proportion of errors on the reversal learning task for both groups per block. Here, no significant difference was found between patients with early-stage AD and controls on the proportion of errors ($F(1, 40) = .089, p = .767, \eta^2_p = .002$), indicating that overall amount of errors did not differ between patients with early-stage AD and healthy controls. However, the proportion of errors significantly differed between the different blocks ($F(2.59, 104) = 10.8, p < .001, \eta^2_p = .212$). Post-hoc tests showed significant effects between Block 1 versus Block 2 ($p = .004$), Block 1 versus Block 4 ($p < .001$), Block 2 versus Block 3 ($p = .005$), Block 2 versus Block 6 ($p = .005$), Block 3 versus Block 4 ($p < .001$), Block 4 versus Block 5 ($p = .004$) and Block 4 versus Block 6 ($p < .001$). That is, the proportion of errors was smaller in the Block 1, 3 and 6 compared to Block 2 and 4 and the proportion of errors was smaller in Block 5 relative to Block 4. No interaction effect between Group and Block was found ($F(2.59, 104) = 2.71, p = .057, \eta^2_p = .063$). These results indicated that patients with early-stage AD adjusted their behaviour over time as much from positive and negative feedback as controls. After the acquisition in Block 1, both early-stage AD patients and healthy controls made more errors during the first and third reversal (i.e. Block 2 and 4), while during the last reversal (i.e. Block 6) they made less errors and adapted their behaviour based on the switched positive and negative feedback.

Additionally, when taking into account, respectively, the first ten trials to which participants responded per block and the first trials per block until participants had given ten correct responses as learning criterion, no differences in performance were found with respect to the ability to adapt behaviour over time in early-stage AD patients compared to controls (First 10 trials: Group: $F(1, 40) = 1.18, p = .284, \eta^2_p = .029$; Block: $F(3.45, 138) = 14.4, p < .001, \eta^2_p = .264$; Block × Group: $F(3.45, 104) = 1.92, p = .120, \eta^2_p = .046$; First trials until 10 correct responses: Group: $F(1, 40) = .099, p = .754, \eta^2_p = .002$; Block: $F(2.98, 119) = 10.8, p < .001, \eta^2_p = .212$; Block × Group: $F(2.98, 119) = 2.54, p = .060, \eta^2_p = .060$). Post-hoc tests showed the same results with the exception of the comparison between Block 2 versus Block 6 in which no significant effect was found ($p > .058$).

Subsequently, we also explored whether the early-stage AD patient differed in their reversal learning abilities compared to healthy controls when only taking into account the two learning conditions, that is, acquisition phase (mean proportion of errors of Blocks 1, 3 and 5) and reversal phase (mean proportion of errors of Blocks 2, 4 and 6) by conducting a repeated measure GLM analysis with Group (early-stage AD vs. controls) as between-subject factor, Learning condition (acquisition vs. reversal) as within-subject factor and proportion of errors as dependent variable. Although no main effect of the proportion of errors made was found between early-stage AD patients and healthy controls, the proportion of errors made during the reversal phase was larger than during the acquisition phase and the difference between the proportion of errors per learning condition was larger in early-stage patients relative to healthy controls (Group: $F(1, 40) = .09, p = .767, \eta^2_p = .002$; Learning condition: $F(1, 40) = 13.4,$
that early-stage AD patients were able to learn to discriminate objects during initial learning, but have more difficulty updating and alter the acquired discrimination rule after the initial stimulus–outcome association was changed relative to healthy controls.

Next, Figure 3d shows the proportion WS and LS responses for both groups. GLM analyses did not demonstrate any difference between the two groups with respect to the extent they applied these heuristic strategies (WS: F(1, 41) = 0.396, p = 0.533, η² = 0.010; LS: F(1, 41) = 0.106, p = 0.746, η² = 0.003). This shows that patients with early-stage AD used the same heuristic strategies, that is, stayed or switched according to previous feedback, compared to controls. In sum, patients with early-stage AD were equally capable as healthy controls in modifying their behaviour based on the overall outcome valence of the trial (i.e. per block) and the previous trial (i.e. WS and LS).

Table 2 shows the Spearman's rank correlation between the recall performance on the Drawer task after EL and TEL and the performance on executive functions and memory tests and the performances on the probabilistic associative reversal learning task. In the patients with early-stage AD a moderate positive correlation for recall performance after EL was found between the proportion of LS responses (r = 0.415), indicating that more often adapting behaviour after negative feedback was associated with worse memory performances after EL. In healthy controls, a large negative relationship was demonstrated between memory (as measured with the Doors Test) and the recall performance task after EL (r = −0.520). This result points out that in controls better episodic memory function is associated with a better performance on the Drawer task after EL.

Additionally, Spearman's rank correlation relating memory, executive functioning, performances on the probabilistic associative reversal learning task and recall performance after EL and TEL in all participants (AD patients and controls taken together) demonstrated strong and moderate negative correlation between memory (as measured with the Doors Test) and later recall after, respectively, EL (r = −0.587) and TEL (r = −0.458). Also, a moderate positive correlation was found between later recall performance after TEL and executive functions (as measured with the Trail Making Test B/A interference score; r = 0.422), indicating that better performance on the Drawer task was in general related to better memory, and better memory performance after TEL was associated with better executive functions.

**DISCUSSION**

In this study, we set out to examine the ability to learn from feedback in individuals with early-stage AD compared to older controls without cognitive impairment. We manipulated the amount of errors that could be made during object-location learning (compared to full EL) and investigated its effect on

| TABLE 2 | The correlations between the distance scores after errorless learning and trial-and-error learning and the performances the Doors Test, Trail Making Test B/A, proportion of errors, proportion of Win-Stay and proportion of Lose-Shift of the probabilistic associative reversal learning task with 95% confidence intervals for each correlation in patients with early-stage Alzheimer's disease (AD) and healthy controls. |
| --- | --- | --- | --- | --- | --- |
| Distance score | Early-stage AD | | | Healthy controls | | |
| | After EL | After TEL | After EL | After EL | After TEL |
| Doors test | −0.410 [-0.742 to 0.159] | −0.246 [-0.588 to 0.332] | −0.520 [-0.842 to 0.056] | −0.371 [-0.712 to 0.035] |
| TMT B/A | 0.273 [-0.306 to 0.901] | 0.435 [-0.025 to 0.854] | 0.130 [-0.343 to 0.537] | 0.346 [-0.123 to 0.710] |
| Proportion of errors (total) | −0.165 [-0.655 to 0.370] | −0.112 [-0.588 to 0.375] | 0.128 [-0.278 to 0.551] | 0.082 [-0.393 to 0.603] |
| Proportion Win-Stay | 0.058 [-0.516 to 0.417] | −0.185 [-0.626 to 0.298] | 0.020 [-0.399 to 0.449] | −0.120 [-0.531 to 0.349] |
| Proportion Lose-Shift | 0.415 [0.155 to 0.863] | 0.330 [-0.063 to 0.795] | 0.200 [-0.346 to 0.425] | 0.134 [-0.421 to 0.591] |

Abbreviations: EL, errorless learning; TEL, trial-and-error learning; TMT, trail making test.
later recall. Also, we examined the participants’ performance on an associative probabilistic reversal learning task.

Our results showed that EL was superior to TEL on later recall of object-location associations, both in patients with early-stage AD and older controls. Moreover, early-stage AD patients benefited just as well from EL relative to TEL as the controls. In addition, after the first error made during the acquisition phase of TEL, making more errors did not have an additional adverse effect on the recall performance. However, patients with early-stage AD, in general, placed the objects in absolute distance further away from the correct location during the recall phase of EL and TEL compared to controls. Furthermore, positive and negative feedback had the same impact on their behaviour accordingly over time in patients with early-stage AD relative to controls. Also, the extent to which early-stage AD patients use heuristic strategies in the probabilistic reversal learning task, that is, stay or switch according to previous feedback, did not differ from the controls. The extent to which early-stage AD patients adjusted their behaviour after negative feedback (i.e. LS) was associated with a worse recall performance of object locations after EL. Moreover, better episodic memory was associated with better recall performance of object location after EL in the healthy controls.

The EL advantage is in line with previous findings of Callahan and Anderson (2019) and Roberts et al. (2018) in individuals with memory impairment due to neurodegenerative disease (i.e., MCI or early-stage dementia). Callahan and Anderson (2019) employed an experimental memory task in which participants with amnestic MCI were given either word-stem cues in the lexical condition or semantic cues in the conceptual condition followed by the target word. They had to write down the target word, repeat the cue-target association aloud and remember the target word. During EL the target word was immediately shown after the cues, whereas during TEL participants always had to make two guesses before the target word was presented. Immediate recall performance after EL was superior to TEL in both conditions. Roberts et al. (2018) found in patients with MCI a beneficial effect of EL for free recall and cued recall using a word-list learning task. In addition, this EL advantage was less salient in MCI patients with better error recognition ability. Also, in learning everyday tasks, an EL advantage was shown in patients with dementia (de Werd et al., 2013). Taken together, the beneficial effect of EL suggests that both patients with early-stage AD and older healthy adults have difficulties in suppressing irrelevant information (i.e. errors) during learning resulting in a larger distance between the selected and correct drawer, with early-stage AD patients having more difficulties in suppressing irrelevant information than healthy adults. From this perspective, irrelevant information may have reduced the ability to encode the relevant information (correct target) or may compete for retrieval with the result that irrelevant information may be retrieved instead of the relevant information and hampering later memory recall. This is consistent with the finding of El Haj (2016) that deficits in controlled inhibitory ability in AD patient hinder to suppress irrelevant information.

Later recall performance in patients with early-stage AD was influenced by whether or not an error occurred during learning, but not by the error frequency. This finding is in accordance with previous findings obtained using the Drawer task in young and older healthy adults, and in patients with acquired brain injury and executive deficits (Schepert et al., 2019, 2021, 2023). Moreover, receiving positive or negative feedback had the same impact on performance in both AD patients and in healthy controls. This finding converges with those obtained by Levy-Gigi et al. (2011) and Gaubert et al. (2022). Levy-Gigi et al. (2011) employed a cue and context reversal learning task in which four playing cards were shown to amnestic MCI patients, who had to flip or skip each card and gain as many points as possible by flipping the cards leading to reward (50% of the presented cards) and skipping the cards leading to punishment (50% of the presented cards). The shape in the middle of the card (i.e. a cross or a dot) represented the cue and the background represented the context. In the reversal phase, cards with a new cue and same context or new context and same cue were shown. Here, the outcome was opposite of the original card of the acquisition phase. Despite an impaired context reversal learning and spared cue reversal learning in patients with amnestic MCI, they demonstrated that this deficit was not influenced by the valence of the outcome and executive deficits. Gaubert et al. (2022) also found that AD patients were as capable as healthy controls in modifying their behaviour during a decision-making task. The result that later recall
was unaffected by error frequency or the valence of the outcome (positive or negative feedback), and that the ability to adjust behaviour based on feedback was unimpaired may indicate that the error-monitoring system is well-functioning in early-stage AD patients and healthy controls. In line, no difference in performance on task requiring executive functions (measured with the Trail Making Test interference score) was found between patients with early-stage AD and healthy controls.

Furthermore, we found that the recall performance after EL covaries with the heuristic strategy LS in early-stage AD patients. That is, early-stage AD patients who are more likely to adjust their behaviour after negative feedback also performed worse on the later recall after EL. This is in accordance with the findings of Ivan et al. (2018) that LS responses were applied to a greater extent in a task with a higher cognitive load in adults compared to adults who were fully attending to the task. In line with the finding of Ivan et al., the relationship between LS and recall performance after EL may be explained by the fact that patients who are cognitively more impaired, are more likely unable to have a relatively higher cognitive load compared to patients who are cognitively less impaired, resulting in worse recall performance. Gaubert and Chainay (2021) reviewed decision-making competence in patients with AD and argued that the decision-making competence of patients with AD seems to converge with cognitive capabilities, where deficits hamper decision-making competence resulting in not being able to modify their strategy. In addition, they stated that decision-making under risk (i.e. the consequences of one's response and the probability of its occurrence are known), such as during our probabilistic TEL task, is especially related to executive functions such as mental flexibility, working memory and inhibition process (see also Delazer et al., 2007; Sinz et al., 2008), whereas decision-making under ambiguity (i.e. the consequence of one's response and the probability of its occurrence is uncertain) is related to long-term memory deficits (see, e.g. Kloeters et al., 2013). Further research is needed to examine whether the relationship between cognitive impairment and heuristic strategies also applies for patients with executive deficits. Likewise, in healthy older adults better episodic memory was associated with better recall performance of object location after EL. This may be explained by the same principle that older adults who in general perform cognitively better also perform better on the Drawer task after EL.

While we found beneficial effects of EL in early-stage AD, there is also evidence that TEL may be more effective than an error reduction approach under certain circumstances. Specifically, the type of task or to-be-learning material may determine whether individuals benefit from either an EL approach or a TEL approach. For instance, TEL may be preferable when errors are semantically related to the to-be-learned information (Bridger & Mecklinger, 2014; Mera et al., 2022). Also, approaches such as retrieval practices have been found superior to EL in individuals with aphasia (Middleton & Schwartz, 2012; Nunn et al., 2023). Cyr and Anderson (2018) argued that EL is especially helpful when information is inflexible and nonconceptual irrespective of age or memory impairment, such as in our Drawer task. However, it should be noted that TEL approaches or retrieval practice has to date not been systematically studied in patients with early-stage AD. Furthermore, the use of strategies (e.g. semantic associations) when placing the objects to help memorizing the location of objects was not prevented. Consequently, participants were free to use any strategy they liked, which mimics everyday task demands. However, we did not observe that any specific strategies were used by the participants and our data showed that all participants adhered to the instruction to place the objects at ‘random locations’ in the drawer.

In sum, the present study demonstrated an EL advantage compared to TEL on object-location memory, although this beneficial effect was not larger in patients with early-stage AD relative to healthy older adults. Moreover, the recall performance was not influenced by the error frequency during learning and positive and negative feedback had the same impact in AD patients compared to healthy older adults. The difference in recall performance between early-stage AD patients and healthy controls may reflect difficulties in acquiring new information in general rather than error monitoring deficits. This, combined with the finding that TEL was found to be associated with executive functioning, may have implication for treatment intervention. That is, reducing irrelevant information in treatment through EL techniques, especially in patients with executive deficits, may be preferable instead of a TEL approach. Further research should examine in what context or form (e.g. verbal or visual) of information
the beneficial effect of EL is cancelled, and which neuropsychological characteristics play a role in this effect in, for instance, more cognitively impaired patients with moderate to severe dementia or a psychiatric disorder with error monitoring deficits such as psychosis (Ettinger et al., 2018; Foti et al., 2021) or psychopathy (Von Borries et al., 2010). Understanding the underlying mechanisms may help to identify which individual will benefit from EL or TEL and facilitate the development or improvement of current treatments.

**AUTHOR CONTRIBUTIONS**

**Inge Scheper:** Study design, analysis, draft writing, and data curation.  
**Inti Brazil:** Study design, analysis, supervision, and manuscript review and editing.  
**Jurgen Claassen:** Patient recruitment, supervision, and manuscript review and editing.  
**Dirk Bertens:** Study design, supervision, and manuscript review and editing.  
**Sofie Geurts:** Patient recruitment, supervision, and manuscript review and editing.  
**Roy Kessels:** Study design, graphs, supervision, and manuscript review and editing.

**ACKNOWLEDGEMENTS**

The authors thank Vitória Piai, Anna Dewenter, Puck Lange, Femke Swartjes and Sevilay Tokgöz for their assistance in collecting the data.

**FUNDING INFORMATION**

R.P.C. Kessels and D. Bertens were supported by the European Regional Development Fund (ERDF/EFRO PROJ-00928).

**CONFLICT OF INTEREST STATEMENT**

None of the authors have any conflict of interest to disclose.

**DATA AVAILABILITY STATEMENT**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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**REFERENCES**


APPENDIX A

A.1 | Instructions of the EL condition of the Drawer task
This appendix consists a written instructions of the EL condition of the Drawer task. The instruction was given to the participants on standard A4 landscape paper and repeated orally.

A.2 | INSTRUCTION
In a moment, you will see a drawer on the screen with an object under it, as shown below.
The idea is for you to place the object in a drawer and remember its location. You can find the correct drawer by hovering the mouse over a drawer you have chosen and using the left mouse button to choose the drawer. If you have chosen correctly, a blue box will appear, and the item will be kept in that drawer. You must remember which drawer each object is kept in, because later you will be instructed to place each object in the correct drawer. There is no time constraint, so take your time to memorize the correct drawer.

Next, a lock will appear on each correctly chosen drawer. This means that these drawers are already full, and you can no longer use them to place new objects.

There are a total of 20 objects and 25 drawers, so some will remain empty. Each object is randomly assigned to a drawer at the beginning of the task, so there is no structure or regularity to which drawers contain
which object. After you put all the objects in the drawers, you can take a break. Then a new round begins in which you must immediately put each object into the correct drawer. So, you should pay close attention to the location of the drawer where each object belongs in the first round! You will not receive feedback in this round and the drawers will not lock. Good luck!

APPENDIX B

B.1 | Instructions of the TEL condition of the Drawer task
This appendix consists a written instructions of the TEL condition of the Drawer task. The instruction was given to the participants on standard A4 landscape paper and repeated orally.

B.2 | INSTRUCTION
In a moment, you will see a drawer on the screen with an object under it, as shown below.

![Image of drawers and an object]

The idea is for you to figure out which drawer the object belongs in and remember its location. You can find the correct drawer by hovering the mouse over a drawer you have chosen and using the left mouse button to choose the drawer. After choosing, a box will appear around the chosen drawer indicating whether your choice is correct or not. If you have chosen the wrong drawer, a red box will appear around the chosen drawer, as shown below. You should then try another drawer for this item.
If you have chosen correctly, a blue box will appear, and the item will be kept in that drawer. You must remember which drawer each object is kept in, because later you will be instructed to place each object in the correct drawer. There is no time constraint, so take your time to memorize the correct drawer.

Next, a lock will appear on each correctly chosen drawer. This means that these drawers are already full, and you can no longer use them to place new objects.
There are a total of 20 objects and 25 drawers, so some will remain empty. Each object is randomly assigned to a drawer at the beginning of the task, so there is no structure or regularity to which drawers contain which object. After you put all the objects in the drawers, you can take a break. Then a new round begins in which you must immediately put each object into the correct drawer. So, you should pay close attention to the location of the drawer where each object belongs in the first round! You will not receive feedback in this round and the drawers will not lock. Good luck!