FORMING NEW ORTHOGRAPHIC REPRESENTATIONS IN ALZHEIMER'S DISEASE AND MILD COGNITIVE IMPAIRMENT

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Abstract

When we read the same word several times, we end up forming an orthographic representation of it that allows us to read it in a fluid way. Several investigations were aimed at how healthy people, children or dyslexic adults learn new words, but little is known on how this process works on patients with neurodegenerative diseases, for example Alzheimer's disease (AD) and mild cognitive impairment (MCI). Hence, the aim of this project was to analyze the formation of new orthographic representations in these people. For that purpose, eight words of a very low frequency were selected, half of them short and half of them long, and were presented six times to the participants, 4 of them in a narrative context. The learning process was measured according to the elimination of the length effect that indicates the crossing from a sublexical reading to a lexical one. The results showed the disappearance of the length effect in the control group, as well as a

reduction in RTs in MCI participants and AD patients, without a disappearance of length effect in these groups. All this indicates that learning was consolidated in the control group, whereas in the MCI and the AD group it cannot be said that a new representation has formed.

Keywords: *Word learning; letter length effect; Alzheimer's Disease; Mild Cognitive Impairment; visual lexicon*.

Introduction

Most of the words that we find when we read a text, whether it is a novel, essay, or newspaper, are familiar, that is, we have seen them many times. But from time to time we find words that are unknown or that we have only seen in rare occasions. The way we read these two types of words is different, as familiar words are read much faster, because we have their representations in our visual lexicon, which allows us to identify all their letters in parallel and read them in a fluid way. In contrast, when we find unfamiliar words, for which we do not have a representation in the lexicon, we read them serially, from left to right. For this reason, the length of the words has an important effect when reading unknown or unfamiliar words, but hardly influences the reading of familiar words. (Weekes, 1997) compared the reading times of frequent and infrequent words and pseudowords, and found that latencies increased with every letter addition in low-frequency words and pseudowords, but did not find this length effect in high frequency words, which were read as fast regardless of how long they were.

On the other hand, when infrequent or unknown words are repeatedly exposed for participants to read, length ceases to have an effect on reading, as the times of long and short words end up converging. This disappearance of the length effect has been used in

numerous investigations as an index to measure the change from a letter-to-letter reading to a parallel reading, or what is the same, to measure the progression from a sublexical to a lexical reading (Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001;
Kwok & Ellis, 2014, 2015; Maloney, Risko, O'Malley, & Besner, 2009; Marinus, Nation, & de Jong, 2015; Suárez-Coalla, Ramos, Alvarez-Cañizo, & Cuetos, 2014; Súarez-Coalla, Álvarez-Cañizo, & Cuetos, 2016). The disappearance of the length effect and the use of the lexical route to read indicates that a new orthographic representation has been incorporated into the lexicon, but how many readings of a word are necessary to form a new representation? Share (1999) found that 7 and 8-year-old children are able to recognize the correct orthographic form of a word after 4 or 6 presentations, when words were included in the context of a story. According to the self-learning hypothesis (Share, 1995), the creation of orthographic representations of words depends on three factors: the knowledge of the relationship between letters and sounds, the phonological sensitivity and the ability to use contextual information. The formation of representations requires a phonological decoding, which allows to learn the specific orthographic information of each word. According to this hypothesis, the repeated reading of infrequent words and pseudowords grants the development of a representation through the association of the written word and its sound, and in turn, the progression from a sublexical to a lexical reading. Further research on this hypothesis also emphasizes the importance of prior orthographic knowledge (Cunningham, 2006; Cunningham, Perry, Stanovich, & Share, 2002) and semantic information (Ouellette, 2010; Ouellette & Fraser, 2009; Suárez-Coalla & Cuetos, 2017; Wang, Castles, Nickels, & Nation, 2011) in the forming of representations.

Using the length effect, Maloney et al. (2009) tested with university students that after 3 or 4 expositions to a new word, the effect of length began to disappear, indicating the creation of representations that concedes parallel reading. Kwok and Ellis (2015) replicated the Maloney et al. (2009) experiment and found a significant reduction of the length effect after 6 or 7 exposures also in English students. In a similar study, with Spanish school-aged children, Suárez-Coalla et al. (2016) found that the length effect was significantly reduced after 6 exposures.

Conversely, it has been seen that people who have difficulties in reading, take longer to form representations in their visual lexicon (Kwok & Ellis, 2014; Suárez-Coalla et al., 2014). Suárez-Coalla, et al. (2014) analyzed this process of creating representations in Spanish children with dyslexia. They found a reduction in the influence of word length after 6 presentations on control participants, however length continued to influence dyslexics across the blocks. These results show that these children have problems when forming orthographic representations of words. These findings were similar to those found in adults with the same problem. Thus, Kwok and Ellis (2014) evaluated the learning of new words in English adults with dyslexia, and their results showed that participants without reading difficulties were able to create a lexical and orthographic representation of the new words after 4 or 5 presentations; nevertheless, adults with dyslexia needed many more repetitions of the word for the length effect to decrease. Furthermore, even when the length effect was reduced, the reading times of dyslexic adults remained much higher than those of the controls, so there also appears to be a less efficient functioning of the lexical route in these individuals.

The process of developing new word representations lasts for a lifetime, as we are finding new words continually, but do older people make representations of new words with the same ease as younger people, or do they need more exposures because of the decrease in brain plasticity with age? It is evident that the learning process in older people is slower than in young people (Fahle & Daum, 1997; Grady et al., 1995; Lövdén, Wenger, Mårtensson, Lindenberger, & Bäckman, 2013; Schenk, Minda, Lech, & Suchan, 2016) but, does something similar occur with the formation of new orthographic representations? Based on the data obtained in people with reading difficulties it is pertinent to ask what happens with older people who are initiating a neurodegenerative dementia? Are they still forming representations of new words? It has been regarded that these patients have problems in acquiring new learning, due to the cerebral atrophy characteristic of their disease (Greene, Baddeley, & Hodges, 1996; Hodges & Patterson, 1995; Sperling et al., 2003). Regarding verbal learning, several studies show that patients with Alzheimer's disease (AD) continue to read correctly even when the disease is well in advance (Arango Lasprilla, Iglesias, & Lopera, 2003; Cuetos, González-Nosti, & Martínez, 2005; Cuetos, Martinez, Martinez, Izura, & Ellis, 2003) but, is their reading preserved only with familiar words, or are they able to form new word representations when read several times?

Although in patients with AD the first symptoms appear at memory level, language problems do not take long to develop. These first alterations manifest firstly in comprehension, both at the level of speech and of reading, especially in low frequency words. This may be due to a deterioration in the functioning of the lexical route, probably at the level of the visual lexicon, since the memory impairment may be affecting the recognition of words. In the study by Arango-Lasprilla et al. (2003) the cognitive impairment of AD patients was evaluated through various neuropsychological tests. Where they found that in the preclinical stages of the disease the patients showed poor performance in the linguistic tasks that required semantic processing, whereas their execution in the language tasks that could be solved by the sub-lexical route was relatively normal. These results are similar to those by Cuetos et al. (2003), who evaluated the language of AD patients with various tests, and found a significant degree of affectation in the tests that required semantic processing, as well as in the reading of pseudowords, and in semantic fluency; however, the word reading performance was quite good in these patients. These authors conclude that the affections observed in semantic processing appears in the early stages of the disease, whereas the problems encountered in reading pseudowords may be explained by an additional deterioration in phonological processing, due to the degenerative nature of the disease. This semantic impairment in patients with AD has also been highlighted in the study by Cuetos et al. (2005), in which a group of patients with AD was assessed repeatedly, using a task of picture naming. Their results show how patients who made semantic errors in the early stages of the disease increased non-response errors as the disease progressed, indicating a loss of concepts.

Between normal aging and dementia, there is an intermediate stage, known as Mild Cognitive Impairment (MCI), which is often identified as the stage leading to the development of dementia. MCI is a clinical entity that was described by Petersen et al. (1999) and has proven to be very useful in detecting people in early stages of AD (Petersen, 2005). According to these authors, people with this type of deterioration differ significantly from healthy people in their memory deficit, but their performance will be equivalent to controls in the other cognitive functions. The functioning of the memory of people with MCI is similar to that of patients with AD, with the distinction that the latter patients also present alterations in the other cognitive functions. At the present time, much has been discussed about the limitations of the term MCI and instead, research has begun to speak of prodromal Alzheimer's (Dubois & Albert, 2004; Molinuevo, Valls-Pedret, & Rami, 2010). Notwithstanding the use of new terminology, MCI will be used in this work.

Given these facts, will MCI patients be able to form new representations of words, or will their memory problem make learning difficult? In a study by Grönholm-Nyman, Rinne, & Laine (2010) it was found that verbal learning was damaged, both in people with MCI and in AD. Its aim was to study the learning of unknown words in both disorders, training the naming through repetitions over a period of four days. The results show a very beneficial effect of semantic support in people with MCI. This indicates preservation of semantic memory, which could be a compensation for its affectation at the level of episodic memory. Patients with AD did not benefit from semantic support. Furthermore, accidental learning and recognition memory were preserved in MCI, presenting a similar performance to controls. In the case of patients with AD, performance was worse as sessions advanced. All participants (AD, MCI and controls) showed the same forgetfulness curve, even though their performance was different. This study concludes that MCI patients learn to name new objects, but their performance is worse than the controls one. The performance of patients with AD, on the other hand, is even worse than that of MCI, due to their coding problems, which prevents them from acquiring new information.

Considering the memory and learning problems of these patients, the aim of this work was to study the process of formation in new orthographic representations in people with MCI and AD, analyzing the number of repetitions they need in order to incorporate new words into their visual lexicon. With regard to determine that the learning has been carried out, the decrease of the length effect in the successive presentations of the stimuli were verified which, as seen, has been used in several investigations as a plausible index to measure the formation of new orthographic representations (Coltheart et al., 2001; Kwok & Ellis, 2014, 2015; Maloney et al., 2009; Marinus et al., 2015; Suárez-Coalla et al., 2014; Súarez-Coalla et al., 2016). According to the results presented in previous studies, it seems reasonable to expect that people with MCI will show a decrease in the length effect, but less than in control participants; whereas in the case of patients with AD, it could be expected that this effect of length remained throughout the presentations, indicating that no new representations have been formed in the lexicon.

Method

Participants

In this study, 63 native Spanish adults participated (34 females and 29 males), with an age range of 63 to 89 years, and a mean of 75.6 years (*SD* = 6.12). All of them knew how to read and write and did not present psychiatric illnesses, neither a history of alcoholism nor drug addiction.

Out of all the participants, 21 were patients from the Cabueñes hospital in Asturias, Spain, diagnosed with AD according to NINCDS-ADRDA criteria (McKhann et al., 1984); another 21 of the participants were elderly people diagnosed with mild cognitive impairment of amnestic type, evaluated by the neurologist at the same hospital. The 21 remaining participants were healthy elderly people and comprised the control group. Most of the participants had primary or secondary education, although some of the participants also had higher education. There were no significant differences between the groups in their educational level or in the age of the participants. All participants were evaluated with the Spanish adaptation of the Mini Mental State Examination (MMSE) (Lobo et al., 1999) and with the Alzheimer's Early Detection Test (Test de Detección precoz de la enfermedad de Alzheimer, TDPA) (Cuetos-Vega, Menéndez-González, & Calatayud-Noguera, 2007). Statistically significant differences were found between the scores of the three groups in both tests: $F(2,60) = 30.94$, $p<0.001$, with an effect size (*partial* $\eta 2 = 0.508$) in the MMSE, and $F(2,60) = 36.54$, $p<0.001$, with an effect size (*partial* $\eta 2 = 0.549$) in TDPA (see Table 1).

Table 1. Summary of participants' characteristics (M, mean; SD, standard deviation).

Group	**AD**	**MC**	**Control**
Female	10	10	14
Male	11	11	7
	M (SD)	***M (SD)***	***M (SD)***
Age	76.61 (7.17)	74.33 (5.39)	76.04 (5.71)
Years of schooling	9.42 (3.59)	9.57 (3.45)	8.47 (1.63)
MMSE	23.47 (2.92)	26.04 (1.82)	28.52 (1.03)
TDPA	43.76 (6.11)	51.89 (9.01)	65.85 (9.85)

Materials

For this study, 8 very low frequency Spanish words were selected, all of them included in the dictionary of the Royal Spanish Academy (RAE). Half of them were short (4 or 5 letters) (e.g., daza) and half long (7 letters) (e.g., papasal). Eight control words, also of very low frequency, paired with the experimental words in terms of length, initial grapheme and first syllable frequency (see Table 2) were also selected.

Table 2. Length and first syllable frequency of the experimental stimuli and of the distracting stimuli.

EXPERIMENTAL	Length	1st Syllable freq.	DISTRACTING	Length	1st Syllable freq.
daza	4	336.25	dacha	5	336.25
duba	4	833.93	dujo	4	833.93
inga	4	133.04	isba	4	42.32
panco	5	96.61	penol	5	4250.71
papasal	7	7122.5	paremia	7	7122.5
rodrejo	7	397.86	raquero	7	636.61
zaranda	7	25	zancajo	7	6
chipojo	7	224.42	chilota	7	224.46

With these stimuli, all unknown to the participants, a reading out loud experiment was designed using the DMDX program (Forster & Forster, 2003). In Phase 1, the 8 experimental stimuli were included, and in Phase 2, in addition to the experimental words, the 8 control words were added. In addition, in both phases, 4 test words and 12-word fillers were shown, which were different in each phase. Test words appeared at the beginning of the experiments, to make sure that participants understood the task. The word fillers where long and short with higher frequency than the experimental words. This experiment was presented to participants in a laptop with an 11-inch screen. The words appeared in 22-point black font, on a white background, in the center of the screen. Before each word appeared, an asterisk was shown on the screen as a fixing point.

A narrative text was also elaborated. It was formed by 4 paragraphs, in each one of which appeared the 8 experimental stimuli, therefore each stimulus was presented a total of 4 times in the narration. In the first paragraph of the text the meaning of experimental words was explained. The text was shown to participants on a white DIN-A4 sheet of paper, with black 14 points lettering. In sum, the 8 experimental words were shown 6 times to the participants.

Procedure

The study was divided into two sessions, to avoid the weariness of participants. In the first session the participants signed an informed consent that guaranteed the confidentiality of their personal data, in accordance with the ethical and privacy regulations required by the code of ethics. The study protocol was approved by the human research committee of the University of Oviedo. Then, they were asked for some personal information (name, age, educational level). After that, they were evaluated with the MMSE (Lobo et al., 1999) and the TDPA test (Cuetos-Vega et al., 2007). This session lasted for about 30 minutes.

In the second session, the reading experiment was conducted. The participants were told to perform reading and memory tasks, and they were asked if they needed glasses to read, and if so, they were asked to use them.

After that, participants were given Phase 1 of the experiment in the laptop. They were told that they should read the words on the screen as fast as they could without mistakes and were also asked to read the instructions of the experiment to confirm that they saw the screen adequately. They were also told that some of the words they were going to see were known, but other words might be unknown to them. They were given headphones with a built-in microphone, as the program generated a sound record for each word of the experiment. Once completed, the participants were presented with the narrative text on a sheet of paper. They were asked to read the text aloud and informed that in this case the important thing was not the speed but understanding what the text was about. Finally, the participants performed the Phase 2 of the reading experiment, following the same steps as in Phase 1. This session lasted about 20 minutes.

Analysis

Recordings generated by the DMDX program (Forster & Forster, 2003) were analyzed with the Check-Vocal (Protopapas, 2007). This software allows to set the reaction times (RTs) of reading manually, based on the spectrogram of each word and its recording. Once this was done, the mean RTs of the experimental words and the control words, as well as the RTs of each participant in each type of stimulus were calculated. Errors [Control 3.7%, MCI 4.36%, AD 5.15%] and non-responses [Control 4.56%, MCI 7.14%, AD 10.11%] were eliminated. Extreme values were also eliminated [Control 2,38%, MCI 1,38%, 2,18%], considering as such those that were two standard deviations above or below the mean. The mean RTs calculated after were analyzed using the SPSS statistical program (version 21.0).

Results

First, a mixed-design analysis of variance (ANOVA) was performed in which all variables were included. The group (control, AD, MCI) was the between-subjects factor; and the experimental phase (Phase 1 and Phase 2) and word length (short and long) were the within-subject factors. A significant effect of the experimental phase was found [*F* (1,57) = 88.712; $p < .001$; *partial* $\eta 2$ = .609], with higher RTs in Phase 1; and a significant effect of length [*F* (1,57) = 60.648; $p< .001$; *partial* η *2* = .516], with higher RTs for long words. No significant effect of the group factor was found, RTs were similar between the three groups in both phases (see Table 3).

Table 3. Mean RTs of the three groups in both phases.

GROUP	**Phase 1**		**Phase 2**	
	Short words	*Long words*	*Short words*	*Long words*
AD	1068.883	1163.072	876.846	1031.315
MCI	1089.892	1136.445	898.975	1042.724
Control	974.275	1097.083	886.303	942.828

We also found a significant interaction between phase, length, and group [*F* (2,57) = 3.904; p = .026; *partial* $\eta 2$= .12]. The control group showed significant differences between short and long words in Phase 1 (p = 0.014), but these differences ceased to be significant in Phase 2, indicating that the length effect present in Phase 1 disappeared after the 6 exposures in Phase 2 in these participants. As for participants with MCI, although they had higher RTs for the long words than for the short ones in Phase 1, these differences were not significant, but they were in Phase 2 (p = <.001), indicating that the length effect was maintained after the 6 presentations in these group. In the case of AD patients, the difference between the RTs in long and short words turned out to be significant in Phase 1 (Figure1) and were maintained in Phase 2 (Figure 2). Nevertheless, the MCI and the AD showed a reduction in their mean RTs.

Figure 1. RTs of the experimental stimuli in the three groups of participants in Phase 1.

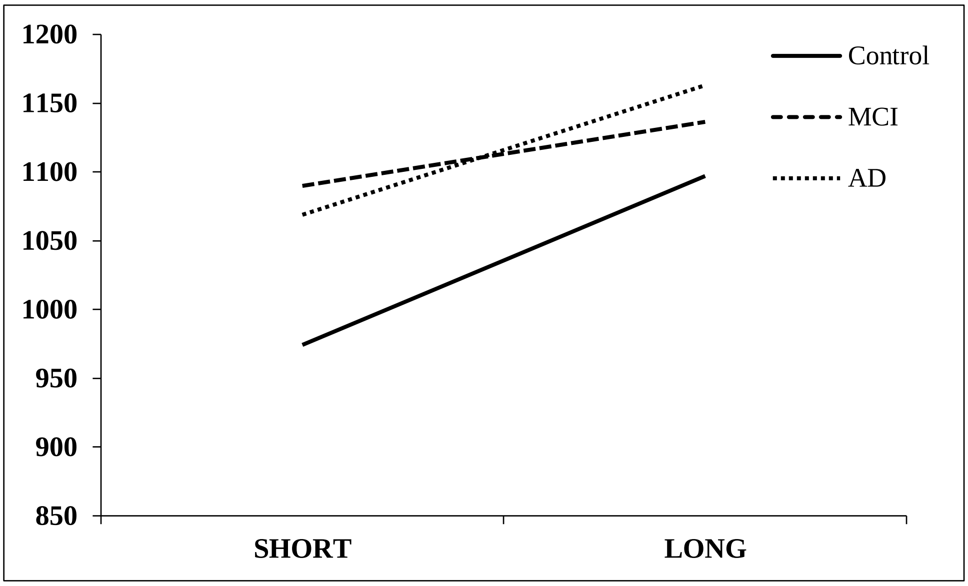
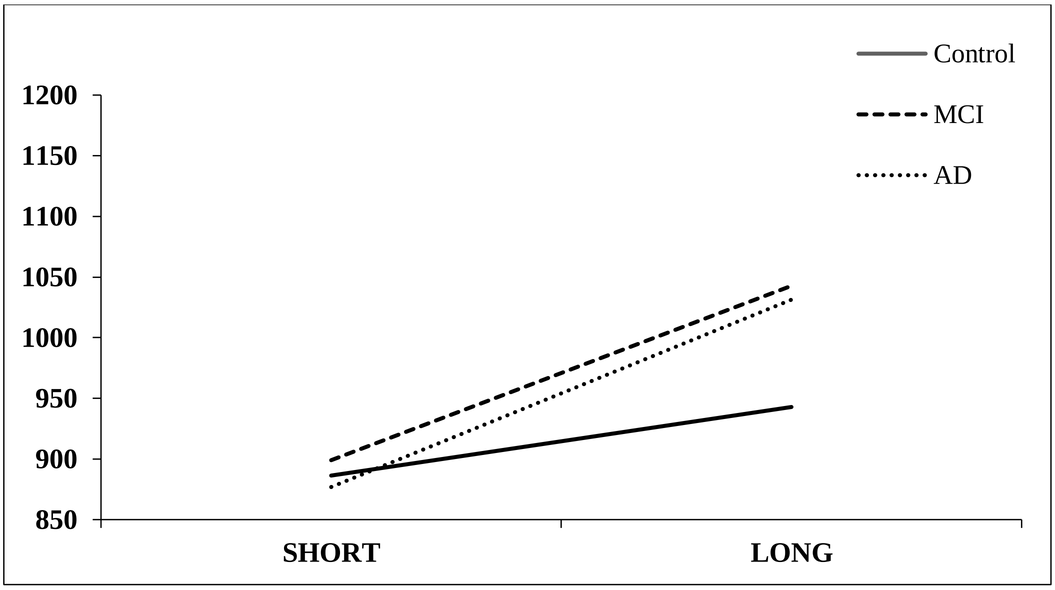


Figure 2. RTs of the experimental stimuli in the three groups of participants in Phase 2.



Performing an ANOVA, the mean RTs of the experimental and distracting stimuli of Phase 2 were compared to verify that there was a length effect on the distracting stimuli, being the first time that they were read, but this effect no longer appeared in the experimental stimuli, which was the sixth time they were presented. The mean RTs in each stimulus were used as the dependent variable, and the group (AD, MCI, control), type of stimulus (experimental, distractor) and word length (short, long) were used as fixed factors. A significant effect of the interaction between type of stimulus and group [F (2,35) = 3.41; p = .044; *partial* $\eta 2$= .163] was found, with significant differences in the RTs of the three groups [Tuckey's pot hoc test (AD-Control, p<.001; AD-MCI, p=.012; MCI-Control, p= .05].

The RTs were higher in the distractor stimuli than in the experimental stimuli in the three groups. Significant differences were found between the RTs of the experimental stimuli and distractor stimuli of the control participants (p = .003), the same difference was found in the patients with AD (p < .001). In the case of the patients with MCI, even though the RTs turned out to be higher for the distractor stimuli, significant differences were not found regarding experimental stimuli, probably caused by the similarity between both types of stimuli. This similarity could be causing a phonological priming effect that impedes the appearance of differences to be expected between the two stimuli. Although mean RTs were lower in the experimental stimuli, the length effect was maintained in Phase2.

Discussion

The aim of this work was to study the process of formation of new orthographic representations in patients with MCI and AD. For this purpose, a reading aloud experiment was designed, which included 8 very low frequency experimental words (4 short and 4 long). To assess the learning, we used the decrease in the length effect, for it has been shown to be a good index to measure verbal visual learning (Coltheart et al., 2001; Kwok & Ellis, 2014, 2015; Maloney et al., 2009; Marinus et al., 2015; Suárez-Coalla et al., 2014; Súarez-Coalla et al., 2016).

Following 6 presentations of the experimental stimuli, the length ceased to influence the RTs of the control participants, indicating the formation of orthographic representations in the new words. The RTs decreased in the MCI participants and AD patients, but there were still differences reading long and short words, so we cannot assure that a new orthographic representation has been consolidated. The performance of the healthy participants went as expected according to the hypothesis proposed by Share (1995), which says that the repeated reading of unknown words results in the formation of new representations, thanks to the association of the written word with its sound, which allows the progression from sublexical reading to a lexical and a more fluent reading. In contrast, repeated word reading did not appear to be sufficient in the case of MCI and AD patients to form a new orthographic representation.

Because of the problems of patients with AD to acquire new learning (Greene et al., 1996; Hodges & Patterson, 1995; Sperling et al., 2003), it was expected to find the length effect in the reading of these participants to remain the same, indicating that no new representations had been formed. The results confirmed this hypothesis. Nevertheless, the RTs of patients with AD did not differ significantly from the other groups in Phase 1 and Phase 2, and their reading accuracy was correct. In this same line were the results gotten by Arango-Lasprilla et al. (2003), who found a significant deterioration in the semantic processing of these patients, but a practically normal sublexical reading. The preservation of this serial reading may be the reason why the RTs of the AD patients were not significantly higher than those of the MCI or the control participants.

As for the results of people with MCI, their performance was similar to the one of patients with AD and worse than that of the control participants. There was a reduction in the RTs on the reading of these participants, but the length effect did not disappear after the 6 exposures, so it cannot be said that these participants are able to consolidate new representations. These results are inconsistent with those described by Grönholm-Nyman et al. (2010), where verbal learning was found to be affected both in people with MCI and AD, but more marked in the latter, since semantic information facilitated the formation of new representations to the patients with MCI, while AD patients did not seem to benefit from this semantic support. In our study, the reading execution was similar in both AD patients and MCI participants.

Many studies have emphasized that providing semantic information favors the formation of new representations (Ouellette, 2010; Ouellette & Fraser, 2009; Suárez-Coalla & Cuetos, 2017; Wang et al., 2011). In our experiment this semantic support was offered to the participants during the reading of a narrative text, because in the first paragraph the meaning of experimental words was explained. It is feasible that this semantic information is the reason why there is a reduction of the RTs of the MCI and AD patients in Phase 2.

Even though the previous MCI reading investigations show a better performance in their memory and learning than AD patients, in this study the performance of both groups were similar. Nevertheless, considering previous studies, it could be expected that increasing the number of presentations the participants with MCI finished forming and orthographic representation, just as it has been reported by Kwok and Ellis (2014) and Suárez-Coalla et al. (2014) in adults and children with dyslexia. These people with reading difficulties showed a reduction in the length effect throughout the presentations but did not totally disappear. It would be interesting to study if the increase in the number of presentations favours people with MCI to form new orthographic representations, and if so, evaluate how many presentations would be necessary for this learning to be consolidated

Although extensive research exists on how new orthographic representations are created in children and adults, little is known about how this process occurs in elderly people with neurodegenerative diseases. The results obtained in this project allow us to know more about the processing of the reading and its deterioration in AD and in MCI. The scarce number of participants and the few stimuli used in the experiment limit this study to generalized results. It would be interesting to be able to consider the stage of the illness in patients with AD, but this was not possible due to reduced samples. Further research would be needed to verify the results obtained. In future research it would be interesting to analyses if the length effect disappears in people with MCI, when the number of presentations are increased, and to elaborate further on how the semantics influence the learning of these participants and AD patients. Knowing more about verbal visual learning in the early stages of neurodegenerative diseases, such as MCI and AD, can help develop compensatory strategies for the problems that these diseases often cause, as well as improving and strengthening the processes that could be preserved in these diseases.

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Disclosure statement

The authors have no declarations of interests to disclose.

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