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Correlations between the performance of older adults in conditional discrimination training and in a screening test for Alzheimer's Disease

Correlação do desempenho de idosos em treino de relações condicionais e em um teste de rastreio para Doença de Alzheimer

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Abstract

The prevalence of neurocognitive disorders has been rising and Alzheimer's Disease (AD) is the most common cause. Studies on conditional discrimination have contributed to understand the variables associated with the cognitive function. However, the relationship of such studies with cognitive impairment in older adults remains under-explored. This research aims to compare the performances of older adults during tasks involving conditional discrimination training with their performances on Addenbroke's Cognitive Examination, a widely used screening test for cognitive impairments. The sample was composed of 45 older adults. The participants performed a computerized task consisting on establishing arbitrary conditional relations between three pairs of stimuli. Addenbrooke's Cognitive Examination was administered to assess the cognitive performance. The analysis revealed a positive correlation between the performance in conditional discrimination and in the cognitive assessment. This correlation was observed only among participants who did not reported having AD in use of anti-cholinesterase drugs (30 participants). These findings demonstrate a direct relationship between learning difficulties, when it comes to learning arbitrary conditional relations, and the occurrence of cognitive decline. Therefore, the administration of the conditional relations tasks could be useful for distinguishing older adults with and without AD.

Keywords: Conditional discrimination; neuropsychological tests; elderly; Alzheimer's Disease.

Resumo

A prevalência de distúrbios neurocognitivos vêm aumentando e a Doença de Alzheimer é sua maior causa. Estudos sobre discriminação condicional vêm contribuindo para a compreensão de variáveis associadas à cognição. Porém, sua relação com alterações cognitivas em idosos ainda é pouco explorada. Este trabalho teve por objetivo comparar a performance de idosos em tarefas de treino de discriminação condicional arbitrário com a performance no teste Addenbroke's Cognitive Examination, um teste amplamente utilizado para o rastreio da Doença de Alzheimer (DA). Participaram do estudo 45 idosos, que realizaram uma tarefa computadorizada de treino de relações condicionais arbitrárias entre três pares de estímulos. Os participantes também passaram pela avaliação cognitiva por meio do Addenbrooke's Cognitive Examination. Observou-se uma correlação positiva entre a performance dos participantes nas tarefas de treino e seus resultados no teste cognitivo. Essa correlação, porém, só foi identificada entre os participantes que relataram não ter diagnóstico de DA e fazer uso de anticolinesterásicos (30 participantes). Esses resultados indicam uma relação direta entre a aprendizagem de relações condicionais arbitrárias e declínios cognitivos. Dessa forma, discute-se que esse tipo de tarefa pode ser útil para o rastreio de alterações cognitivas em idosos.

Palavras-chave: teste neuropsicológico; discriminação condicional; idosos, Doença de Alzheimer.

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Studies have reported an increase in the prevalence of neurocognitive disorders (NCD) in Brazil. Alzheimer's Disease (AD) is the main cause of NCD (Chaimowicz, 2009). AD is a neurodegenerative disease that leads to the progressive impairment of cognitive functions, particularly remembering (American Psychiatric Association, 2013).

Over recent years, conditional discrimination has been used to study memory and cognitive repertoires in AD diagnosed patients in a behavior analytic approach (Ducatti & Schmidt, 2016; Sartori, 2008; Souza, 2011; Steingrimsdottir & Arntzen, 2011a, 2014). In most cases, experimenters have exposed participants to matching-to-sample (MTS) tasks. In this procedure, usually a sample stimulus is presented (e.g., A1 or A2) with, at least, two comparison stimuli (B1 and B2); a selection response is required in each trial. The comparison defined as correct varies according to the sample presented. For instance, when A1 is the sample and B1 and B2 are comparison stimuli, the selection of B1 is considered as the correct response (the same for B2 given the sample A2). Literature results point out that older adults with AD usually perform poorly in such tasks (Ducatti & Schmidt, 2016; Steingrimsdottir & Arntzen, 2011b, 2014)

For example, Ducatti and Schmidt (2016) used an exclusion procedure to teach arbitrary conditional discriminations to older adults with and without AD. All the participants without AD learned the conditional discriminations between A and B, and A and C stimuli, but none of the participants with AD learned any of the conditional discrimination relations. Therefore, the same procedure that was efficient in teaching arbitrary conditional discrimination to older adults without AD, did not yield the same results for participants with AD. In a second experiment, participants with AD were able to learn arbitrary conditional discrimination when a delayed-cue procedure was included.

Ducatti and Schmidt (2016) also tested the emergence of equivalence classes in Study 1. In stimulus equivalence classes, after learning at least two arbitrary conditional relations (baseline relations), the characteristics of equivalence relations can be measured by testing the reflexive, symmetrical and transitive relational properties (Sidman & Tailby, 1982). In reflexivity, the relation between a stimulus and itself is true (ArA, in which “r” represents relation). In symmetry, direct training occurs from the relation of one stimulus to a physically different stimulus and the AB relation is established, with the emergence of a symmetrical relation between B and A (if ArB, then BrA). In transitivity and symmetrical transitivity, relations emerge between stimuli that have never been directly related but are related to a common stimulus (if ArB and ArC, then BrC and CrB), which are also denominated equivalence relations.

In Study 1, Ducatti and Schmidt (2016) aimed to establish four 5-member equivalence classes. As none of the participants with AD learned the baseline relations, the tests for derived relations were not carried out with them. When it comes to the participants without DA, three out of five of them demonstrated the emergence of the derived relations.

Some studies have investigated the relationship between the performance of older adults in the emergence of equivalence classes and other procedures for cognitive decline screening (Arntzen & Steingrimsdottir, 2017; Gallagher & Keenan, 2009). Gallagher and Keenan (2009) investigated the relationship between the scores on the Mini Mental State Examination (MMSE; Folstein et al., 1975) – a screening test for cognitive impairment in which lower scores are related to lower cognitive abilities – and the performances of older adults on a task involving the formation of two 3-member equivalence classes. The experimenters used a MTS procedure to, first, test reflexivity, train AB and BC relations, and test symmetry and equivalence. Half of the participants did not learn baseline relations (arbitrary conditional discrimination) or did not demonstrate the emergence of symmetry. These were the participants with lower MMSE scores. Although correlation scores were not calculated, the results seem to point out to a relationship between the performance on stimulus equivalence tasks and the MMSE score.

Arntzen and Steingrimsdottir (2017) also found evidence that cognitive decline – measured based on electroencephalographic activity – was related to the non-emergence of symmetrical relations (Arntzen & Steingrimsdottir, 2017). In an exploratory study, four older adults learned AC and BC baseline relations and were tested for the emergence of symmetrical (CA and BC) and equivalence relations (AC and CA). The performances on these tasks were compared to Electroencephalography (EEG) records of these participants. The experimenters were especially interested in The Ach Index, retrieved from the EEG. A low Ach Index has been correlated with a higher probability of Mild Cognitive Impairment (MCI) (Johnsen et al., 2014). The two participants that did not respond in accordance with the stimulus equivalence were also the ones with lower Ach Index; and the one participant who showed an Ach Index consistent with a MCI, was the only one who did not achieve the criteria in the symmetry test.

Results from Gallagher and Keenan (2009) and Arntzen and Steingrimsdottir (2017) suggest that there might be a correlation between the performance of older adults in equivalence classes formation tasks and in cognitive measures. However, the literature shows that disruption in performances of older people with cognitive impairments can be seen not only in the emergence of stimulus equivalence properties, but as early as in the training of baseline relations (Ducatti & Schmidt, 2016; Steingrimsdottir & Arntzen, 2011b, 2014). Heading from this, this research aims to compare the performances of older people during tasks involving conditional discrimination with their performances on Addenbroke's Cognitive Examination, a widely used screening test for cognitive impairments, to verify if there are correlations between these performances.

Methods

Participants

51 individuals were recruited from primary care units and meetings for older adults. Participants were discharged when they presented: a) vision or hearing impairment, b) severe clinical or psychiatric comorbidities, c) a history of stroke reported by the patient or family and d) evidence of depressive symptoms [identified by five or more points on the short-version of the Geriatric Depression Scale, GDS-15 (Almeida & Almeida, 1999)]. Therefore, the sample was composed of 45 older adults (19 men and 26 women, $M = 74.4$ years old, SD=8,42), ranging 60-95 years old. This study was approved by the Human Research Ethics Committee (certificate number: 66233817.8.0000.5504).

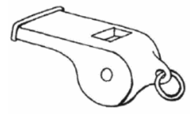
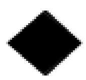
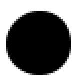
Materials and Setting

The session was conducted at the participants' houses and lasted about 20 minutes. Sociodemographic data were collected during interviews with the participants and/or family. The questions addressed date of birth, sex, age, marital status, occupation, education and address. The GDS-15 (Almeida & Almeida, 1999) was used to evaluate signs of depression. This instrument is a short version of the GDS (Sheikh & Yesavage, 1986) and it is used as a screening tool for depression in older adults. It is composed of 15 "yes/no" questions with a cutoff of 5 points.

The Addenbrooke's Cognitive Examination – revised version (ACE-R) was used to evaluate the cognitive profile of the participants. This short group of tests has been translated and cross-culturally adapted to be used in Brazil (Carvalho & Caramelli, 2007). The ACE-R includes items from the MMSE and has been widely used to detect cognitive disorders. The measurement consists of the following cognitive domains: attention and orientation; memory; verbal fluency; language; and visuospatial abilities. In the Brazilian version, the cutoff for the detection of AD is of 78 points, with 100% of sensitivity and 82.26% of specificity (Amaral-Carvalho et al., 2015).

The conditional discrimination training task was performed using a portable, touchscreen computer with a 13-inch touch screen (Dell®, model 7348) and the Superlab 4.0 software (Cedrus corporation®). All stimuli were visual and were presented on the computer screen. Stimuli from the pre-training block were composed of two pictures of fruits and two Japanese letters. The training and testing of conditional relations involved two sets comprising three pictures each; Set A: A1 – tree, A2 – house, A3 – whistle, taken from the Boston Naming Test (Kaplan et al., 1983) and Set B: B1 – rhombus, B2 – circle, B3 – triangle (See Table 1).

Table 1
Stimuli Used in the Conditional Discrimination Tasks.

Sets of stimuli	Classes		
	1	2	3
A			
B			

General Procedures

Sociodemographic data were collected, followed by the administration of the GDS-15 (Sheikh & Yesavage, 1986). Next, the ACE-R was carried out, followed by the conditional discrimination training blocks.

MTS Pre-training

In the pre-training, conducted to make the participants familiar with the task and the equipment, the participants received an audio instruction about how to perform the task and the experimenter demonstrated how to do so. The task took 10 to 15 minutes.

At the beginning of the task, the instruction was “Hello. You will participate in a test in which you will learn to relate figures. Your task will be as it follows: In each attempt, there will always be one figure at the top and one or more figures at the bottom of the screen. You should look at the figure at the top and choose among the figures at the bottom the figure that is related to it. The program will teach you which figure is the correct one. When you get it right, colored stars will appear on the screen. When you make a mistake, the screen will turn white. Shall we make some attempts to learn?”

In the second, third and fourth trials, the instructions were, respectively: “You should respond like this: First, look at the picture at the top. Now, notice that a figure has appeared at the bottom. Tap the figure at the bottom.”; “Now, you will have one more attempt. First, look at the figure at the top. Now, notice that two figures appear at the bottom. Only one of them is related to the figure at the top. Tap on it.”; and “Now, you will have the last attempt to learn how to respond to the task. First, look at the figure at the top. Now, notice that three figures have appeared at the bottom. Only one of them is related to the figure at the top. Tap on it.”

The pre-training exposed the participants to MTS tasks. In all MTS trials, the sample stimulus was presented centered in the upper part of the screen. Following an interval of 2s, two stimuli were presented in the lower part of the screen, equally distributed. The participants selected a comparison stimulus by touching one of them on the computer screen. The selection of the comparison stimulus defined as correct in a given trial (e.g., given Y1, selecting X1) was followed by stars appearing on the screen for 2s. Incorrect responses were followed by a 2s blank screen. Once the feedback was over, another trial automatically started. In every block, the position of the comparison stimuli in the lower part of the computer screen was randomized (left, center, right).

At the beginning of the pre-training phase, the first two MTS trials presented the correct comparison stimulus circled in red. These trials were repeated until the participant chose the correct comparison in both of them; then, six new trials with the same pair of stimuli were presented without the visual cue.

AB Relation Training

In AB baseline training, MTS trials (identical to the ones in the pre-training but, then, the audio instruction was removed) were used to teach A1B1, A2B2 and A3B3 relations in a block comprising 36 trials with feedback (12 trials per relation). As in the pre-test phase, the first time each relation was presented (in this case, in the first three trials), the correct comparison was circled in red. But there were no criteria to move to the next trials. The first 18 MTS trials presented two comparison stimuli and, the last 18 ones, three comparison stimuli. The participants performed all the trials, regardless of their performances, so that there would be no differences in the number of trials among participants, and the performances could be compared to the scores in the ACE-R. After finishing this training block, the experimenter thanked the participant, and the procedure was over.

Statistical Analysis

The SPSS 21.0 version was used for all statistical analyses. The averages of correct responses for the trials of each set of stimuli (A1B1, A2B2, and A3B3) in the MTS task for each group (see Results section) were compared in a Student’s T-Test for independent samples. The correlation between the performances in the MTS task and the screening test scores for the ACE-R and for the MMSE was assessed by the Pearson’s correlation coefficient ($p < .05$ as an indicative for statistical significance).

Results

Among the 45 participants included in the experiment, 15 of them reported having AD and using anti-cholinesterase drugs. They will be called Group 1. The 30 participants who did not report having AD nor using anti-cholinesterase drugs will be called Group 2. Table 2 presents the socio-demographic information and clinical data stratified per group. Groups 1 and 2 only differed for their respective cognitive assessment (ACE-R and MMSE) scores. Considering each domain, differences were observed in memory and attention/orientation scores.

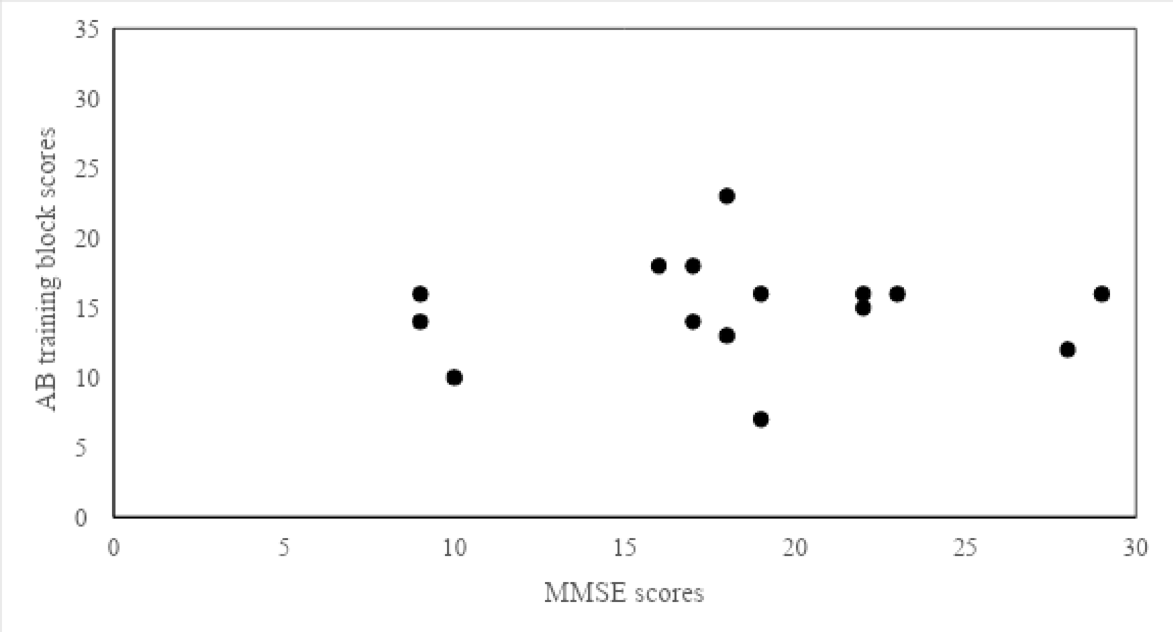
Table 2
Demographic and Clinical Data Stratified by Group.

	Group 1 (n=15)	Group 2 (n=30)	X2/t; *p*
Sex (M/F)	7/8	14/16	X^2=0.00; 1.00
Age (years)	76.33 (±6.67)	73.50 (±7.89)	t_{43}=1.19; 0.240
Schooling (years)	5.33 (±5.34)	5.93 (±5.24)	t_{43}=0.36; 0.721
MMSE	18.40 (±6.03)	23.86 (±4.08)	t_{43}=3.59; 0.001
ACE-R	47.86 (±16.90)	67.00 (±19.99)	t_{43}=3.17; 0.003
Domains			
Attention/orientation	11.26 (4.18)	14.56 (2.44)	$t_{18.9}$=2.82; 0.011
Memory	7.93 (3.59)	15.76 (5.96)	$t_{41.3}$=5.47; <0.001
Verbal fluency	4.46 (3.18)	6.53 (3.36)	t_{43}=1.97; 0.054
Language	14.80 (6.01)	18.66 (6.19)	t_{43}=1.99; 0.053
Visuospatial	9.40 (3.46)	11.53 (3.89)	t_{43}=1.79; 0.080

Figure 1 and 2 present the participants' performances in the AB training blocks and the scores in the MMSE and the ACE-R. The performances in the AB training blocks ranged from 7 to 35 correct answers. The average of correct answers in Group 1 was of 14,93 (SD=3,96) and of 22,6 (SD=7,27) in Group 2. There was a significant difference between the groups (t42,96=4,48; p<0,001). The performances in Group 1 ranged from 10 to 35 correct responses and the performances in Group 2 ranged from 7 to 23 correct responses. Eight participants from Group 2 presented more than 85% of correct responses. In Group 1, the highest performance was of 67% of correct trials for one participant. Participants from Group 1 performed poorly in the AB training, regardless of their scores in the MMSE or in the ACE-R.

Figure 1
Group 1 Performance in AB Training Block in Correlation with the MEEM's Score (a) and ACE-R Score (b).

(a)



(b)

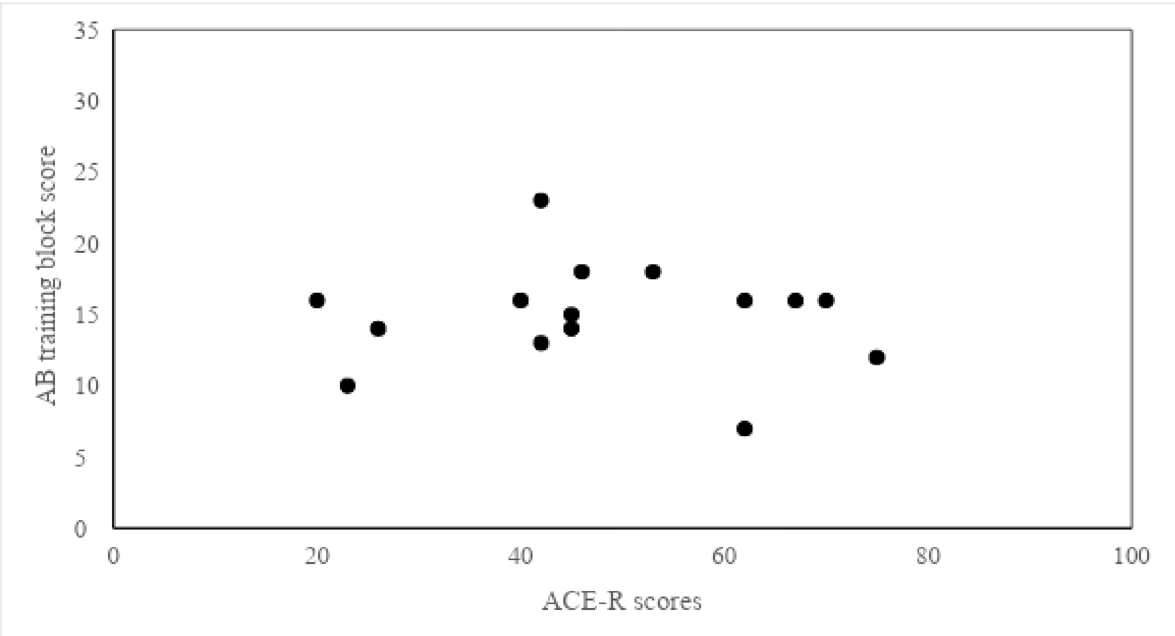
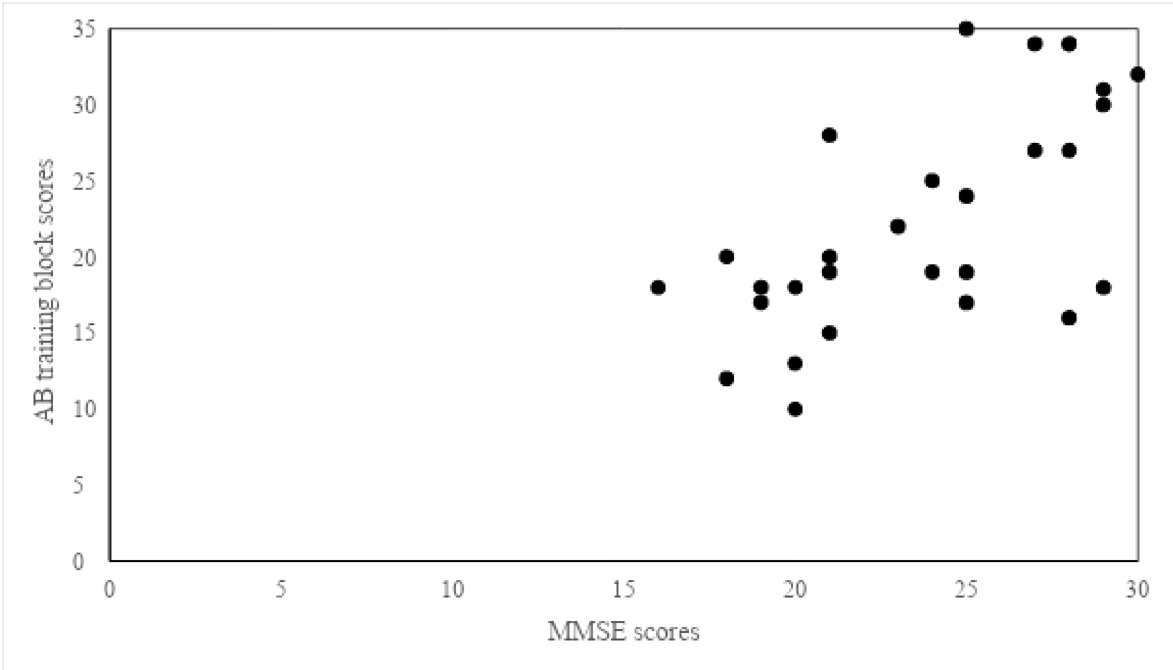


Figure 2

Group 2 Performance in AB Training Block and in the MMSE (a) and ACE-R (b).

(a)



(b)

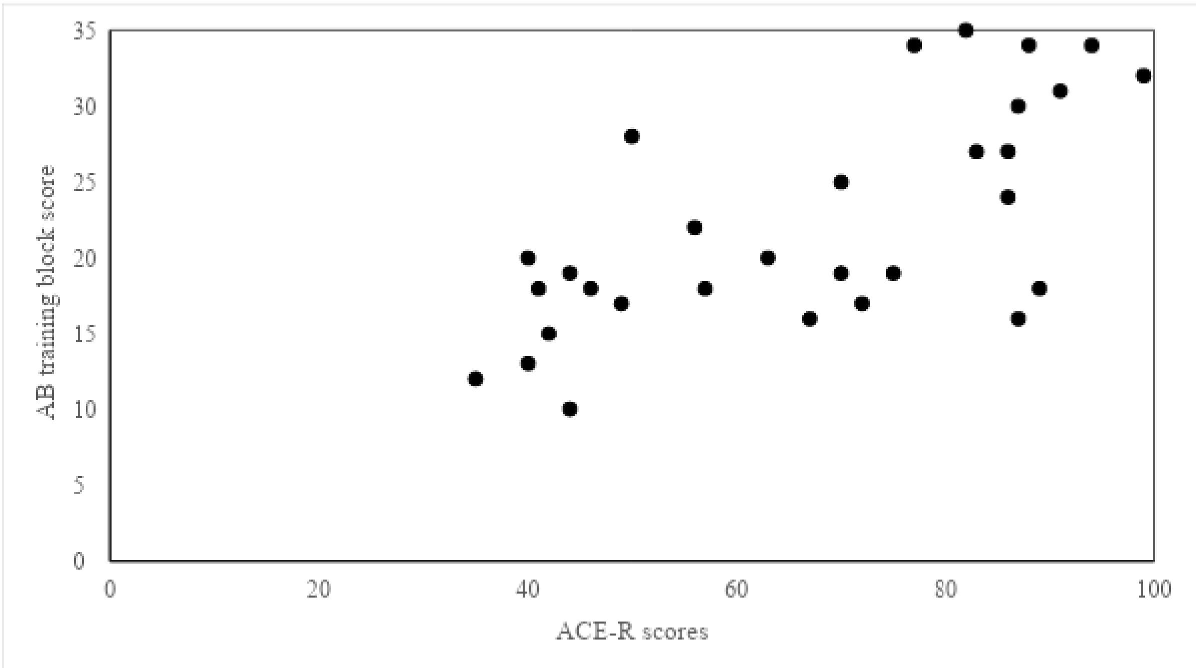


Figure 3 depicts the performance of each participant, in each trial of the AB training. Correct responses are represented with a dark (participants from Group 1) or medium gray square (participants from Group 2). Incorrect responses are represented with an empty space. The red line separates trials with two and three comparison stimuli. 14 participants from Group 2 performed better with two comparison stimuli, 11 participants presented more correct responses in trials with three comparisons (the second half of the block) and five of them had the same number of correct responses with two and three comparison stimuli. Among the 15 participants who reported having DA, 14 of them performed better in the trials with two comparison stimuli and only one of them showed a better performance in the second half of the block.

Figure 3

Correct (Medium and Dark Gray) and Incorrect (Empty Spaces) Responses from Each Participant in AB Training Block. C Indicates Group 2, and AD, Group 1.

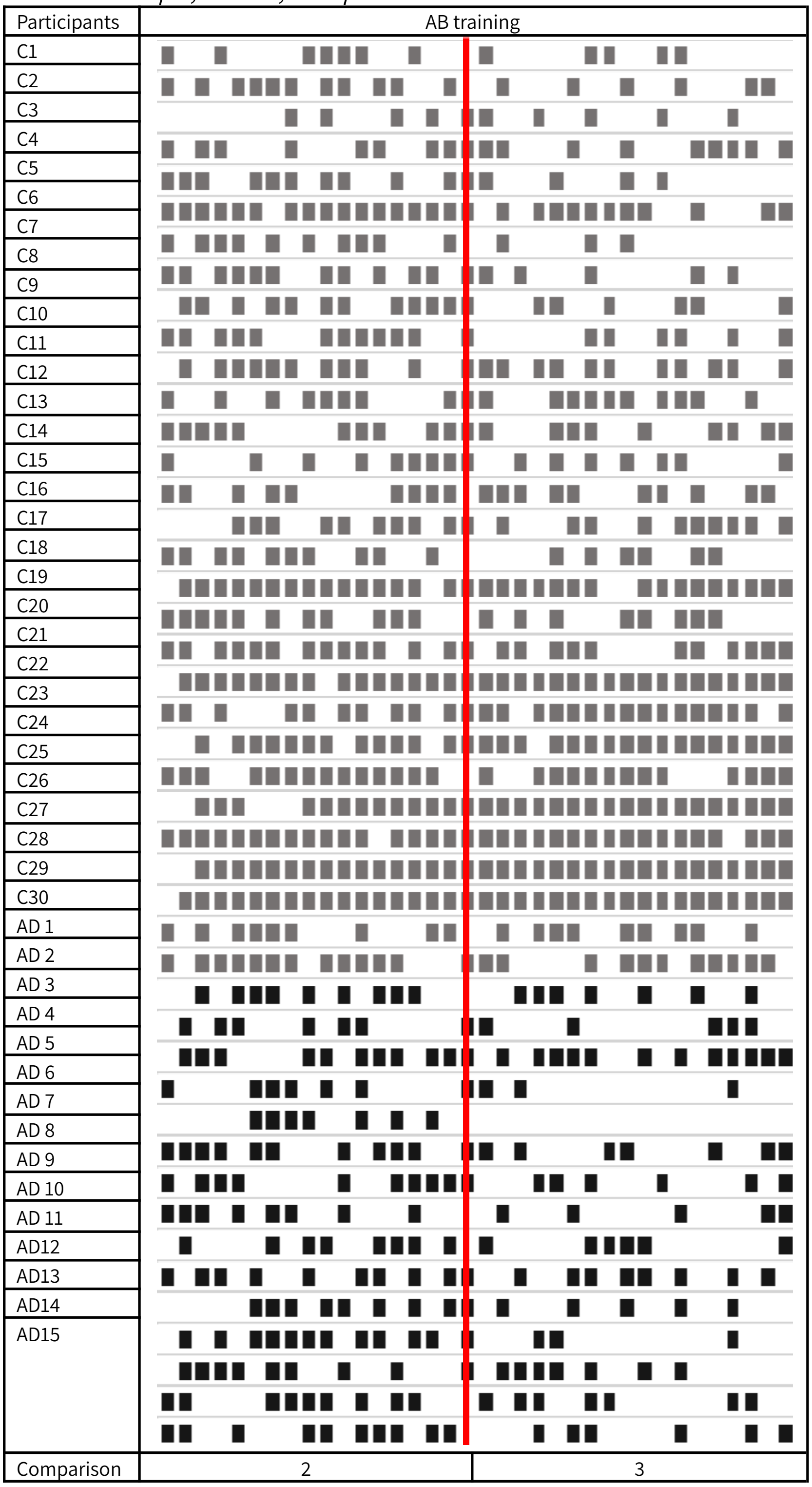


Table 3 displays the correlation between the performances in the AB training and the demographic and clinical characteristics of the sample. There was a positive moderate correlation between the performances in the AB training and the scores in the MMSE and ACE-R, and a small correlation with years of schooling. Considering only the participants in Group 2, there was a positive moderate correlation between the performances in the AB training block and the years of schooling, and the scores on the MMSE and ACE-R. In contrast, there were no correlations between the variables among the participants in Group 1.

Although we did not assess the formal diagnosis of AD, sensitivity and specificity were calculated based on the number of correct responses in the AB training block to identify AD causes (considering self-reported AD diagnoses). The best balance was found at a cutoff point of 16 correct responses, achieving 80% of sensitivity and 80% of specificity.

Table 3
Correlations Between the Score on Conditional Discrimination Training (AB) and Cognitive Measurements.

	Group 1 (n=15)	Group 2 (n=30)	All (N=45)
MMSE	r=0.049 p=0.861	r=0.602 p<0.001	r=0.547 p<0.001
ACE-R	r=-0.058 p=0.837	r=0.688 p<0.001	r=0.644 p<0.001

Discussion

The main goal of this study was to determine correlations between the performances of older adults in conditional discrimination training and the results of traditional cognitive assessment measurements. The correlation analyses revealed directly proportional relationships between the AB baseline training performances, and both the MMSE and ACE-R. When sorting the participants into those who reported having, or not, AD diagnoses and taking, or not, anti-cholinesterase medication, a moderate correlation was observed only for Group 2.

Although the literature shows that older adults without cognitive impairments can learn arbitrary conditional discrimination training (Aggio & Domeniconi, 2012; Ducatti & Schmidt, 2016; Steingrimsdottir & Arntzen, 2014; Wilson & Milan, 1995), such outcome with AD diagnosed participants has been considered as a challenge (Aggio, 2021; Ducatti & Schmidt, 2016; Gallagher & Keenan, 2009; Steingrimsdottir & Arntzen, 2011a). Ducatti and Schimdt (2016) showed that the same procedure used to teach conditional discrimination to older adults without AD failed to achieve the same result with older adults with AD. In Gallagher and Keenan (2009), the same procedure to establish equivalence classes yielded different results in participants with and without cognitive impairments; the first showing worse performance. In Steingrimsdottir & Arntzen (2017), participants were neither diagnosed with AD nor with cognitive impairments, but the electroencephalographic activity pointed out to early signs of cognitive impairments for one participant. Although this participant learned the conditional discrimination relations, she was the only one who failed to demonstrate the emergence of symmetrical relations. In our results, participants from Group 1 performed worse than the ones from Group 2. Combined with the latest results, this finding may indicate that one's performance on a learning task of such type is correlated with cognitive decline and future investigations could seek to understand whether or not the performance in such task is a predictive of cognitive decline.

It is noteworthy that, although the results showed that higher scores in the MMSE and ACE-R were positively correlated with a better performance in the AB baseline training considering all of the participants; when individually analyzing participants who reported, or not, having AD, this correlation was only observed among participants in Group 2. This seems to have two important implications. First, apparently, even when older adults with AD get a satisfactory performance on these traditional cognitive measurements, they do not have the same success when it comes to learning conditional relations. Second, this also seems to indicate that, although having cognitive impairment may result in a lower performance in conditional discrimination, this kind of task is not sensitive to the degree of impairment. Despite their performances in the ACE-R test, all participants from Group 1 performed poorly in the AB training tasks. These findings may suggest that learning conditional discrimination tasks, by itself, may be sufficient with respect to screening for AD, but not for its stage. It is noteworthy that it is not possible to understand whether the lower performance in the MTS is, in fact, coming from the lack of conditional discrimination or in even simpler repertoires, such as simple discrimination (simultaneous or successive). Future research should keep this investigation moving by including simpler tasks and a formal diagnosis of AD.

As for the sensitivity of conditional discrimination tasks to screening for AD, the cutoff point of 16 correct answers in the AB training set corresponded to 80% of sensitivity and specificity. These results are similar to the 100% of sensitivity and 82.26% of specificity of the cutoff point of 78 in the ACE-R for AD screening in general population (Amaral-Carvalho et al., 2015) and the 89.2% to 90% and 71.7% to 79.8% of specificity for the Clock Drawing Test (Aprahamian et al., 2009), which is also commonly used for dementia screening. Likewise, the results for sensitivity and specificity are similar to those found by the MMSE (Santiago-Bravo et al., 2019). It should be clear that this study only collected self-reported data about DA diagnoses. Other measurements could have yielded different results. Therefore, we believe it is worthwhile to continue the investigation on the potential of the conditional discrimination training trials as a screening tool for Alzheimer, as future research could access a formal DA diagnosis.

Results also indicated a positive correlation between the performances in AB training block and years of schooling. This correlation was stronger for Group 2. Years of education are an important variable when analyzing participants' scores in the MEEM and ACE-R. In Brazil, the cutoff point for such assessments is different considering the participants' years of education (Brucki et al., 2003; Carvalho & Caramelli, 2007). Nevertheless, we are not aware of any study that indicated such relation with respect to the performance in a conditional discrimination relation for older adults. This relationship should further be investigated and data about the participant's years of education should be collected in research involving such task with elder participants.

It is worth to mention that the proposed task has advantages over other cognitive screening tests, such as the fact that it can be easily implemented in digital format, which enables to screen large populations in a fast and low-cost procedure. Moreover, performing a digital task minimizes the interference of the evaluator on the performance of the individual being evaluated.

An important difference from our study to others found in the literature is that we did not establish a learning criterion nor provided the participants with the opportunity of repeating the training blocks. This was an important aspect, because the comparison between the performance in the AB training and the ACE-R one required that there were no differences in the number of trials performed by each participant. Some variables were included to facilitate the training, such as the pre-training, the inclusion of familiar stimuli, the gradual increase in the number of comparison stimuli (from two to three) and the cues in the first trials of the AB training. If we consider 85% of correct responses as an indicative that the participant learned the conditional discrimination, this would mean that none of the participants in Group 1 achieved the learning criteria and that 26,6% of the participants in Group 2 achieved it. We cannot say that these results corroborate others from the literature (e.g., Ducatti and Schmidt, 2016), because other studies provided participants with the opportunity of repeating the test; therefore, such comparison is not possible. We can say the same about the difference of performances in trials with two and three comparison stimuli. Some papers reported that participants with AD performed better in trials with two comparisons (Aggio et al., 2021; Steingrimsdottir & Arntzen, 2011b); in our experiments, all participants in Group 1 and almost half of the ones in Group 2 performed better in trials with two stimuli. Nevertheless, we cannot say that this corroborates with the literature. Future studies could manipulate other variables to increase or decrease the likelihood of learning AB relations and evaluate whether this would change the correlation with the ACE-R.

The literature demonstrates that older adults with AD have difficulties learning arbitrary conditional relations (Gallagher & Keenan, 2009; Ducatti & Schmidt, 2016; Steingrimsdottir & Arntzen, 2011b) and this experiment is the first one to find a direct correlation between the performance on conditional relation tasks and scores on cognitive tests. We believe that the results can contribute to better understand the acquisition of stimulus control, especially involving arbitrary conditional discriminations and its relation with cognition impairments in older adults. It also indicates a possible new screening tool for cognitive decline, especially in patients with Alzheimer's Disease.

Future investigations should address some of the limitations of our study, such as increasing the sample in order to increase the generalization of the results, accessing formal diagnoses of AD, investigating the capacity of the conditional discrimination tasks to distinguish between AD and other forms of dementia, and longitudinal studies should investigate whether the decline in learning capacity is an essential factor and an early sign of the emergence of AD.

Declaration of Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Contribution of each author

All the authors have equally contributed to complete the manuscript.

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