

Dual task in healthy elderly, depressive and Alzheimer's disease patients

Dupla tarefa em idosos saudáveis, depressivos e pacientes com doença de Alzheimer

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ABSTRACT

Objective: To investigate whether the DT performance can be affected by the diagnosis of major depressive disorder (MDD) and Alzheimer's disease (AD). **Methods:** Cross-sectional data with 108 individuals [Healthy (HE) = 56, MDD = 19, AD = 33] aged 60 and older of both sexes diagnosis with AD, MDD, and HE without a clinical diagnosis of mental disorders, residents of the city of Rio de Janeiro. DT performance, was measured by mean velocity (m/s), DT cost and the number of evoked words ($DT_{animals}$). One-way ANOVA was used to compare groups. In addition, a logistic regression was used to verify the association between the performance in the DT variables and the risk of MD and AD, controlled by age and scholarity. **Results:** There was a significant difference between the HE and AD groups in the DT variables. The worst performance in the DTC and $DT_{animals}$ variables increased risk of AD, regardless of age and scholarity (DTC, OR = 5.6, 95% CI = 1.4-22.2, $p = 0.01$ and $DT_{animals}$, OR = 3.6, 95% CI = 0.97-14.0, $p = 0.05$). **Conclusion:** The ability to perform two tasks simultaneously appears to be impaired in patients with Alzheimer's disease, and unaffected by the major depressive disorder.

Keywords

Cognitive function, dual task, Alzheimer's disease, depression, functional capacity.

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RESUMO

Objetivo: Avaliar o quanto o desempenho em dupla tarefa pode ser afetado pelo diagnóstico do transtorno depressivo maior (TDM) e pela doença de Alzheimer (DA). **Métodos:** Estudo de corte transversal com 108 indivíduos [Saudáveis (IS) = 56, TDM = 19, DA = 33] com 60 anos ou mais, de ambos os sexos, diagnosticados com doença de Alzheimer, transtorno depressivo maior e sem diagnóstico de doenças mentais, residentes na cidade do Rio de Janeiro. O desempenho em DT foi avaliado pela velocidade média (m/s), custo da dupla tarefa (CDT) e número de animais evocados por segundo ($DT_{animais}$). ANOVA *one-way* foi feita para a comparação dos grupos. Além disso, foi utilizada uma regressão logística para verificar a associação entre o desempenho nas variáveis em DT e o risco de TDM e DA, controlado pela idade e escolaridade. **Resultados:** Houve diferença significativa entre os grupos IS e DA nas variáveis em DT. O pior desempenho no CDT e no número de animais evocados em DT aumentou o risco de DA, independentemente da idade e escolaridade (CDT, OR = 5,6, IC de 95% = 1,4-22,2, $p = 0,01$ e $DT_{animais}$, OR = 3,6, IC de 95% = 0,97-14,0, $p = 0,05$). **Conclusão:** A capacidade de realizar duas tarefas de forma simultânea parece ser prejudicada em pacientes com doença de Alzheimer e não afetada em pacientes com TDM.

Palavras-chave

Função cognitiva, dupla tarefa, doença de Alzheimer, depressão, capacidade funcional.

INTRODUCTION

Major depressive disorder (MDD) and Alzheimer's disease (AD) are highly prevalent in the elderly, and there is a bidirectional relationship between them, since MDD may be a risk factor for AD, but the inverse pattern could also occur and vice versa¹, since areas such as prefrontal cortex and hippocampus are affected in both diseases^{2,3}. According to Butters *et al.*⁴, this relationship can be explained by different ways: 1) HPA axis dysregulation that leads to increased cortisol levels, leading to hippocampal atrophy; 2) ischemic damage in the frontal-striatal regions. In addition, Kessing and Andersen⁵ found that the higher the number of episodes of major depression, increase the chance of this patient progress to a diagnosis of dementia. In Brazil, MDD has a prevalence of 7%⁶ and more than half of the Brazilians identified with dementia are diagnosed with AD⁷, establishing a major economic impact on the lives of these individuals and their families^{8,9}. According to Araujo *et al.*¹⁰, a decreasing cognition gradient is observed when comparing healthy elderly, elderly with depression, patients with AD and elderly people with AD and MDD in comorbidity, wherein the relationship between the decline of cognitive functions and progress of both diseases is already well-established.

As a result, there has been a mounting interest in evaluation ways that are able to recognize AD and MDD, and efforts to find tests which lead to early recognition of both diseases¹¹⁻¹⁴. Tests using an individual's ability to perform two simultaneous tasks, named dual task (DT) have been used to address functional independence in a more naturalistic way. Gait analysis combined with a cognitive or motor task is one of the most used procedure. DT has been based on the hypothesis that when performing two tasks at the same time, in which similar neurofunctional circuits

are recruited, an interference between them will be caused, resulting damages in the performance of one or both tasks¹⁵. Recently, the DT test was chosen to make the base battery for the assessment shared of mobility and cognition from the Canadian Consortium on Neurodegeneration in Aging (CCNA) and was considered sensitive to evaluate motor and cognitive changes, as well as being applicable in research and clinical practice¹⁶.

Interference between simultaneous tasks has been observed in the gait of the young, the elderly, and patients with different diseases¹⁷⁻²⁰. In addition, there is an association of a better gait performance in DT with different health parameters, such as the lower risk of falls in individuals with a better gait performance in DT, as well as the relationship between more active individuals and a better velocity in DT^{21,22}. Likewise, DT tests has been suggested to evaluate cognition due to lower influence of educational level²³. Lastly, comparisons between Health Elderly and those with neuropsychiatric diseases, such as MDD and AD, have been studied²⁴⁻²⁶, being increasingly suggested the use of DT walking tests as a way of early identifying the signs of these diseases. Recently, Montero-Odasso *et al.*²⁷ concluded that elderly with mild cognitive impairment (MCI) with a high DT cost (>20%) are more likely to progress to dementia. Metzger *et al.*²⁶ compared four groups: acute depressed plus cognitively mildly impaired, acute depressed, cognitively mildly impaired and health control, and found that health control group was the fastest in DT tests in comparison to other groups.

Based on the fact that MDD and AD are high prevalent diseases in the elderly, and both are related to a decline of physical and cognitive functions, the present study aimed to investigate Dual Task performance in elderlies with MDD and AD. Our hypothesis is that subjects with AD present a worse performance in every DT variables in comparison to HE subjects.

METHODS

A cross-sectional study designed to compare the performance in DT of subjects who are healthy, depressed, and with Alzheimer's. The sample consisted of individuals aged 60 and older of both sexes diagnosed with AD, MDD, and HE without a clinical diagnosis of mental disorders, residents of the city of Rio de Janeiro. The AD diagnostic evaluation occurred according to DSM-IV²⁸ and to NINCDS-ADRDA²⁹, including mild or moderate degrees according to Clinical Dementia Rating (CDR)³⁰. Patients with MDD were also diagnosed with DSM-IV criteria. Patients with mild to moderate MDD were included according to the Brazilian version of the Hamilton Depression Scale³¹. The elderly diagnosed with AD and MDD were being treated at the Center for Alzheimer's Disease and other Disorders of Old Age at the Institute of Psychiatry of the Federal University of Rio de Janeiro. Health elderlies were all those who did not present diagnostic criteria for both diseases. Elderly who are illiterate or with a physical comorbidity that made it impossible to perform tests were excluded, as well as older people diagnosed with depression in a remission state or score ≥ 25 points in Hamilton Scale (HDRS) for MDD and subject classified as CDR 3 according to the Clinical Dementia Rating (CDR) for AD. All those evaluated completed a medical history and performed physical, cognitive, dual task tests and anthropometric measurements [body mass index (BMI)], and signed the written informed consent form, and had access to all relevant research information and the main researcher's contact information. The evaluations were carried out on two distinct days and they lasted approximately 1 hour. The study was approved by the Research Ethics Committee at IPUB-UFRJ, under the following CAAE registration number: 24904814.0.0000.5263, and is part of the main research project titled "Efficacy of physical exercise in the treatment of major depression, Alzheimer's Disease, and Parkinson's Disease", which was registered under the Brazilian Registry of Clinical Trials (REBEC) protocol RBR-4M3K2C.

Mini Mental State Exam

The MMSE was used to evaluate the general cognitive state, analyzing capacities of orientation (spatial and temporal), attention, concentration, memory, calculation, and language^{32,33}.

Physical function

To evaluate physical capacity of the elderly, three tests were used: 1) 30 seconds chair stand test, which evaluates the lower body muscle strength, requiring the individual to perform the highest number of full stands in 30 seconds³⁴; 2) 2 minutes Step test, which evaluates the cardiovascular endurance, the evaluated individual should elevate each knee to a point midway between the patella and the iliac crest³⁴; 3) 8 foot up

and go test which aims to evaluate the agility and dynamic balance, requiring to get up from seated position, walk 8 foot, turn, and return to seated position on chair³⁴.

Dual task analysis

The DT test used was a combination of the 8 foot up and go test and the verbal fluency test. The subjects should perform the 8 foot up and go test with the maximum possible efficiency in the shortest possible time while evoking the highest number of animals they could. The instructions were as follow: "Please walk as fast as you can, do not run, and evoke the highest number of animals you could". For DT performance analysis, the mean velocity in the 8 foot up and go test in DT (DT m/s), the dual task cost (DTC), which was calculated by the formula $(DTC = ([\text{time of the test in a single task} - \text{time of the test in a dual task}] / \text{time of the test in a single task}) \times 100)$, and the number of the animals named per second during the performance of the 8 foot up and go (DT_{animals}). To determine the cut-off points of the variables in DT, the 25th and 75th percentile values found in the sample were used as classification criteria. Thus, performances $\leq 25^{\text{th}}$ percentile, between 26-75, and > 75 , were classified as below normal, normal, and above normal, respectively.

Statistical analysis

To verify the normality of the data, the Kolmogorov-Smirnov analysis was used. To compare the groups (AD_{mild}, AD_{moderate}, MDD, and HE), one-way ANOVA and a Bonferroni post-hoc test for comparison between group pairs in the variables that presented normal curves were performed. For the variables that did not present normal curves, the Kruskal-Wallis and the Mann-Whitney U analysis were used. To verify if the MDD and the AD groups were clinically different from the HE group the effect size calculation in DT variables was used ($effect\ size = ES$)³⁵. Finally, with the aim of analyzing the chance of elderly individuals with different diagnoses presenting a worse performance in the variables in DT, a multinomial logistic regression was performed. For logistic regression analysis, DT performance was used as independent variables, all of which were categorized into three outcomes (Performance $\leq 25^{\text{th}}$ percentile, Performance between the 26th and 75th percentile, and Performance $> 75^{\text{th}}$ percentile) and the different diagnoses were used as dependent variables. Secondly, the same predictive model was adjusted for age and education in order to verify whether these variables could influence the result. The statistical program SPSS version 20 was used for data analysis and the accepted significance level was $p \leq 0.05$. The sample size calculation was performed and found that the sample had an observed power $> 80\%$ ($\beta = 0.99$), thus having external validity.

RESULTS

The sample consisted of 189 subjects, 81 subjects being excluded for different reasons, totaling 108 older people divided into three groups, 56 HE, 19 diagnosed with major depression disorder (MDD) at a moderate stage (HDRS = 16.92 ± 4.60) and 33 with Alzheimer's disease (AD) (22 with AD_{mild} and 11 with AD_{moderate}). Figure 1 shows the recruitment description of subjects. Table 1 shows that the AD_{mild} group was slightly older, with a significant difference compared to the HE group ($U = 334.00$, $p = 0.002$) and MDD group ($U = 108.50$, $p = 0.008$), and they had a lower educational level compared to the HE group ($U = 310.00$ and $p = 0.001$). The AD group, as expected, presented a worse performance and a significant difference in MMSE compared to the HE ($p < 0.001$) and MDD groups ($p < 0.001$).

It was possible to observe a lower limb strength and agility and mobility above the cut-off point for risk of functional loss in the MDD and AD groups, evaluated by the "Sit Chair Stand test" and "8 foot Up and Go test", respectively. In the "Step 2 minutes test", only the HE group presented a performance above the cut-off point for risk of functional loss, while the other groups presented a performance below the cut-off point. Significant differences between the groups in "8 foot Up and Go test" ($X^2 = 10.43$ e $p = 0.015$), and "2 minutes Step test" ($F = 3.22$ e $p = 0.026$) were observed, and in the "8 foot Up and Go" test only the mild and moderate AD groups were significantly different from the HE group (HE X AD mild $U = 379.00$; $p = 0.008$; HE X AD moderate $U = 162.00$; $p = 0.013$). Table 1 shows the characteristics of the sample.

Differences were observed among groups in the mean velocity (m/s) ($F = 11.09$; $p < 0.001$), in the DTC ($X^2 = 22.35$;

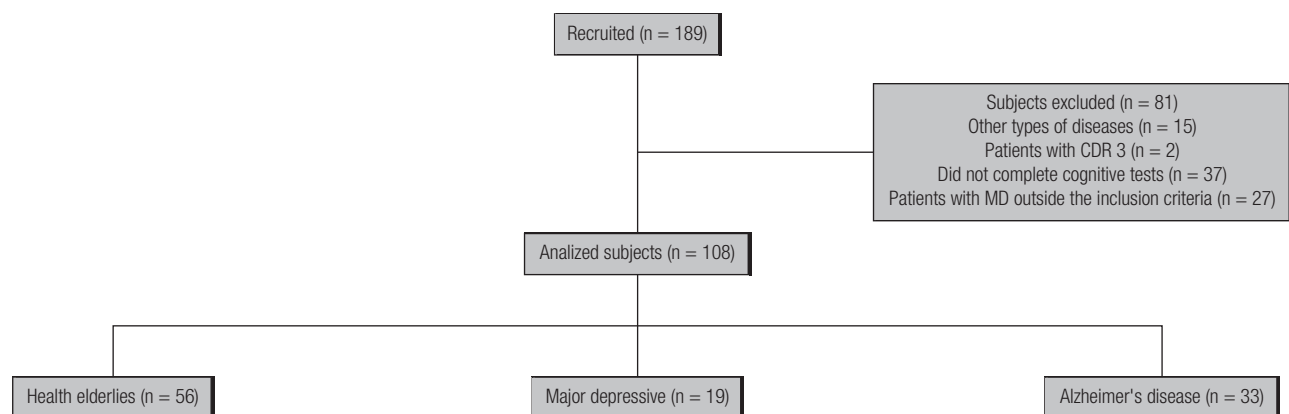


Figure 1. Fluxogram of sample recruitment.

Table 1. Clinical characteristics of the patients

	HE (n = 56)	MDD (n = 19)	AD Mild (n = 22)	AD Moderate (n = 11)	F/X ²	p
Age (years)*	68.50 (60-93)	67.00 (60-88)	75.00 (64-80)	73.00 (60-80)	11.81	0.008^{a,c}
Education (years)*	12.50 (1-29)	11.00 (4-20)	7.50 (3-22)	12.00 (2-16)	13.32	0.004^{a,c}
BMI (kg/m ²)*	25.52 (20-40)	25.74 (20-33)	24.84 (19-38)	24.07 (19-29)	2.4	ns
HAM -D	-	16.92 (4.60)	-	-		
Cognitive Variables						
MMSE (Score)*	29.00 (22-30)	29.00 (22-30)	22.50 (17-28)	19.00 (11-22)	62.00	< 0.001^{a,b,c,d,e}
Verbal Fluency (number of animals)	17.66 ± 4.25	16.16 ± 3.57	11.90 ± 4.90	9.82 ± 4.64	16,00	< 0.001^{a,b,c,d}
Stroop Test points (Score)*	16.00 (11-35)	15 (11-21)	24.31 (13-53)	35.55 (19-61)	34.15	< 0.001^{a,b,c,d}
Trails A (sec)*	53.00 (22-169)	46.18 (37-94)	104.08 (50-181)	131.00 (59-181)	27.25	< 0.001^{a,b,c,d}
Digit Spam backward (Score)	5.00 (2-10)	3.50 (2-12)	3.50 (2-6)	3 (0-8)	12.27	0.007^{a,b}
Physical Function Variables						
Sit Chair Stand (rep)*	12 (8-21)	11 (8-18)	11 (8-18)	12 (7-17)	6.84	ns
8 foot up and go (sec)*	6.10 (4-9)	6.70 (4-15)	7.13 (4-16)	6.91 (6-19)	10.43	0.015^{a,b}
2 min Step (rep)	78.66 ± 23.07	62.33 ± 30.72	64.11 ± 24.04	62.09 ± 31.25	3.22	0.026

* Non-parametric variables described in median, minimum and maximum values.

BMI: body mass index; HAM-D: Hamilton Scale; MMSE: Mini Mental State Exam: ^a Significant differences between healthy elderly and AD mild ($p < 0,01$); ^b Significant differences between healthy elderly and AD moderate ($p < 0,01$); ^c Significant differences between major depression and AD mild ($p < 0,01$); ^d Significant differences between major depression and AD moderate ($p < 0,01$); ^e Significant differences between AD mild and AD moderate ($p < 0,01$). AD: Alzheimer disease; MDD: major depressive disorder; HE: healthy elderly.

$p < 0,001$), and in $DT_{animals}$ ($F = 11.56; p < 0,001$). The AD group presented a worse performance regardless of staging in comparison to the HE group in the three variables analyzed ($p < 0.001$). When comparing between the MDD and AD groups, only the $AD_{moderate}$ group presented a significant difference in the three variables [mean velocity (m/s) ($p = 0.03$), $DT_{animals}$ ($p < 0.001$), and DTC ($U = 39.00, p = 0.004$)], while the AD_{mild} group presented a significant difference only in DTC ($U = 123.00, p = 0.025$). The results of the comparison of DT variables in the different groups are presented in table 2.

Effect size showed that the MDD group presented worse performance than HE group. Although the effect size small and moderate was observed in the three DT variables (mean velocity (m/s), $d = -0.39$; DTC, $d = -0.57$; $DT_{animals}$, $d = -0.20$) in MDD, large clinical differences (AD_{mild} : mean velocity (m/s), $d = -1.19$; DTC, $d = -1.12$; $DT_{animals}$, $d = -0.81$) and ($AD_{moderate}$: DT(m/s), $d = -1.49$; DTC, $d = -1.81$; $DT_{animals}$, $d = -1.86$) were observed in the AD_{mild} and $AD_{moderate}$ groups (Figure 2).

Table 3 shows the results of the logistic regression analysis. By dividing groups into three classifications, it was possible to observe that a performance below the 25th percentile did not increase risk of MDD compared to the HE group. However, a performance below this percentile in the DTC increased risk of AD diagnosis in 3.6 times (OR =

3.6, 95% CI = 1.04-12.67, $p = 0.042$), while in the $DT_{animals}$ the probability increased to 4.2 times (OR = 4.2; 95% CI = 1.14-15.56; $p = 0.031$). A performance below the 25th percentile in the mean velocity (m/s) variable did not increase risk of AD. These results remained after adjusted by age and scholarly ($DT_{animals}$: OR = 3.6; 95% CI = 0.97-14.0; $p = 0.05$ and DTC; OR = 5.6; 95% CI = 1.4-22.2; $p = 0.01$).

DISCUSSION

The present study aimed to compare the DT performance among healthy, MDD and AD elderlies. In addition, we analyzed the chance of elderly individuals with worse performance in DT parameters presenting a diagnosis of AD or MDD.

As expected, mild and moderate AD presented a worse performance in DT compared to healthy older adults and the impairment in DT was associated with the severity of disease. Our results, corroborate the study from Beauchet *et al.*³⁶, that verified an association between the increase of the severity of cognitive impairments with a decrease of different gait parameters. A possible explanation is the relationship between the performance in different subfunctions

Table 2. Comparison of performance in dual task between groups

	HE (n = 56)	MDD (n = 19)	AD Mild (n = 22)	AD Moderate (n = 11)	F/X ²	p
Dual Task (m/s)	0.68 ± 0.12	0.61 ± 0.21	0.49 ± 0.22	0.43 ± 0.11	11.09	<0.001 ^{b,c,e}
Number of animals (animals per second)	0.85 ± 0.30	0.79 ± 0.29	0.59 ± 0.32	0.32 ± 0.18	11.56	<0.001 ^{b,c,e}
Dual Task Cost (%)*	-16.71 (-63.89-8.92)	-15.16 (-169.19-10.07)	-39.98 (-196.28-5.39)	-39.39 (-138.95-18.08)	22.35	<0.001 ^{b,c,d,e}

* Non-parametric variables described in median, minimum and maximum values. ^b Significant differences between healthy elderly and AD mild ($p < 0,01$); ^c Significant differences between healthy elderly and AD moderate ($p < 0,01$); ^d Significant differences between major depression and AD mild ($p < 0,01$); ^e Significant differences between major depression and AD moderate ($p < 0,01$); ^f Significant differences between AD mild and AD moderate ($p < 0,01$). AD: Alzheimer disease; MDD: major depressive disorder; HE: healthy elderly.

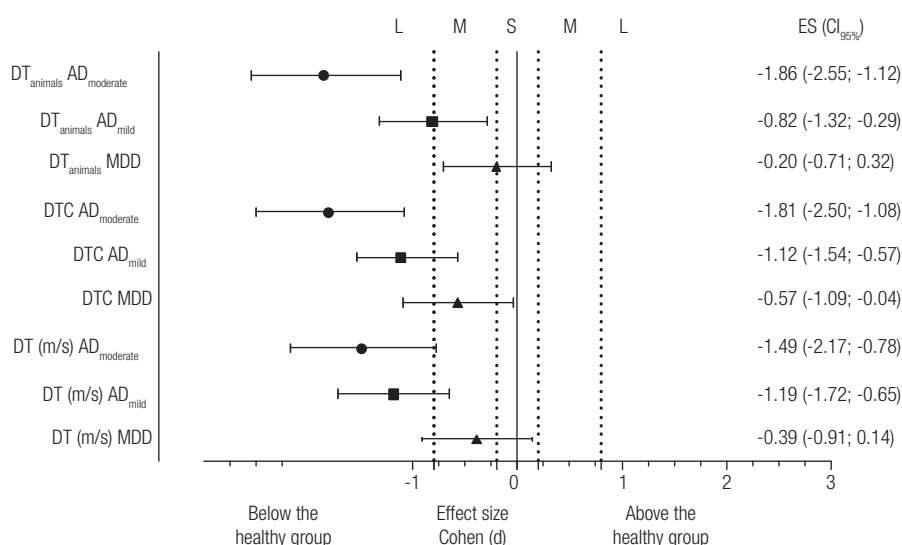


Figure 2. Effect size of the DT variables of the MDD and AD groups. The reference values used are the mean values of the DT variables (DT(m/s), $DT_{animals}$ and DTC) found in HE group. S = Small (< 0.20); M = Moderate (0.21-0.80); L = Large (0.80).

associated with executive functions (EF) and the performance of DT^{19,37,38} and by the association between divided attention deficits and metabolic dysfunction of right frontal and parietal lobes in AD patients³⁹. These findings reinforce theories that consider DT as a way of assessing the ability of the brain to divide attention. In this sense, Beauchet *et al.*¹¹ suggested the use of DT tests by combining gait with a second task as a way to evaluate an early dementia diagnosis. In the present study, the AD group presented a worse performance in all DT variables compared to the other two groups, in addition to presenting a worse clinical performance compared to the healthy group thus corroborating the studies above. Our study suggests that the worse performance in DT seems to be associated with the cognitive impairment caused by AD. Another aspect that supports the hypothesis of a worse performance in DT being a clinical characteristic associated with patients with AD, is the increased chance of diagnosis with the presence of a performance below the 25th percentile being only observed in this group.

DT performance was not affected by MDD. The similar performance of MDD and HE groups in performing the dual task can be explained by a similar global cognitive performance assessed by the MMSE, besides presenting preserved physical capabilities. The performance of activities in DT requires a greater activation of brain areas when compared to a single task, mainly in the prefrontal cortex¹⁷, which demands that these areas are preserved. Even in elderly diagnosed with depression, cognitive and

physical functions were not impaired by the disease, to the point of clinically and significantly interfering in the ability of performing tasks in DT. Another point to note is that all patients diagnosed with depression used selective serotonin reuptake inhibitors (SSRIs). Paleacu *et al.*⁴⁰ showed that SSRIs, besides reducing depressive symptoms, were also able to increase the distance covered by approximately 13.2 meters in the test that evaluated gait performance. The results found in the present study partially corroborate, which found a significant difference between depressed and non-depressed elderly only in DTC and in DT tests with greater complexity. Moreover, Radovanović *et al.*⁴¹ found changes in few gait variables (gait cycle time and double support time) of depressive patients, and they also observed a prioritization of attention to gait during the more complex task (gait + subtraction of 7+ carrying a tray with a glass of water). It is possible that the relatively simple DT protocol used in the present study did not generate an enough cognitive demand to impair performance in MDD patients. This study has some important limitations. The cross-sectional design did not allow the establishment of cause-effect interferences in DT variables. Another point that can be considered a limitation of the study is the fact that the sample is part of a group that intended to receive treatment and may somehow influence the outcome of the study. We suggest in future studies, it was also investigated CDT related cognitive task, as this could increase the understanding of the behavior of AD patients during testing in DT.

Table 3. Association between DT performance and major depressive disorder and Alzheimer disease diagnosis

	MDD			AD			MDD†			AD†		
	OR	(95% CI)	p	OR	(95% CI)	p	OR	(95% CI)	p	OR	(95% CI)	p
DT (m/s)												
Between the 25 th and 75 th percentile	1			1			1			1		
Below the 25 th percentile	0.73	(0.18-3.0)	0.67	3.2	(0.86-11.83)	0.08	0.55	(0.11-2.5)	0.45	1.7	(0.41-7.7)	0.43
Above the 75 th percentile	0.27	(0.02-2.6)	0.26	0.87	(0.11-6.6)	0.9	0.23	(0.02-2.3)	0.21	0.83	(0.09-7.0)	0.87
DT Animals												
Between the 25 th and 75 th percentile	1			1			1			1		
Below the 25 th percentile	0.51	(0.12-2.1)	0.35	4.2	(1.14-15.56)	0.03*	0.47	(0.11-2.0)	0.32	3.6	(0.97-14.0)	0.05*
Above the 75 th percentile	0.21	(0.02-2.0)	0.17	1.9	(0.29-12.5)	0.48	0.26	(0.02-2.5)	0.24	2.1	(0.30-15.3)	0.43
DTC												
Between the 25 th and 75 th percentile	1			1			1			1		
Below the 25 th percentile	1.6	(0.40-6.4)	0.49	3.6	(1.04-12.6)	0.04*	1.9	(0.42-8.7)	0.39	5.6	(1.4-22.2)	0.01*
Above the 75 th percentile	1.15	(0.27-4.9)	0.84	1.3	(0.19-8.7)	0.77	1.2	(0.27-5.4)	0.84	1.6	(0.23-11.5)	0.62

DT (m/s): mean velocity in DT; DTC: dual task cost; DT_{animals}: number of animals evoked in DT; MD: major depressive; AD: Alzheimer disease. * Significant result. † Adjust by age and scholasticity.

CONCLUSION

In conclusion, the ability to perform two tasks simultaneously appears to be impaired in patients with Alzheimer's disease, and unaffected by the Major Depression.

INDIVIDUAL CONTRIBUTIONS

José Vinícius Ferreira, Narahyana Bom de Araujo and Andrea Deslandes – Contributed to conception and design of data. Msc.

José Vinícius Ferreira, Felipe de Oliveira, Jéssica Plácido, Paula Sant' Anna, Renato Sobral Monteiro-Junior, Valeska Marinho, Jerson Laks and Andrea Deslandes – Contributed to revising it critically for important intellectual content. All authors reviewed and had given the final approval of the version to be published.

CONFLICT OF INTERESTS

All authors declare none conflict of interest. This research project was registered under the Brazilian Registry of Clinical Trials (REBEC) protocol RBR-4M3K2C.

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