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## Neuropsychological and Physical Trajectories in Neurotypical and High-cognitive Performing Older Adults

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ABSTRACT

The maintenance of high cognitive performance in old age has increasingly become a public health interest due to associations between cognition, well-being, longevity, and autonomy. The objective of the research is to investigate cognitive, physical, and psychological trajectories of neurotypical older adults (NOAs) and high performing older adults (HPOAs). An exploratory study to investigate 21 NOAs and six HPOAs (mean age 71, SD = ± 3.59), followed up for one year. The older adults were submitted to physical fitness, quality of life, anxiety, depression, RAVLT, ACE-R, and Stroop tests, being assessed at three moments: baseline, six months after the cognitive (MEMO) or stimulation (Stimulus) interventions, and six months after the multimodal interventions, which could be physical or psychopedagogical interventions (health education lectures). Nonparametric statistical tests (Mann-Whitney and Wilcoxon) were performed with  $p \leq 0.05$ . The results demonstrated that the cognitive measures were good predictors of cognitive performance and we observed positive correlations between cognitive and mood measures. The older adults with high performance had a lower prevalence of depressive symptoms. There were gains in global cognitive performance, mood, and in physical fitness variables associated with multimodal interventions, evident in the neurotypical group.

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## 1. Introduction

The maintenance of high cognitive performance in old age has increasingly become a public health interest due to associations between cognition, well-being, longevity, and autonomy. However, according to Randolph<sup>[1]</sup>, most studies published in this field still focus on cognitive decline and only a minority focus on investigating normal or increased cognitive performance in old age<sup>[2]</sup>.

Over the last two decades, a better understanding of the profile of high-performing older adults (HPOAs) generated a growing interest in the field of aging neuroscience, being proposed the term SuperAgers which was originally operationalized in the Northwestern Program, based on the following criteria: individuals over 80 years old; episodic memory performance equal to or above that of cognitively typical individuals between 50-60 years old; performance in cognitive domains of non-mnemonic functions at least on the average for their age<sup>[3,4]</sup>.

Theoretical constructs about older adults with a greater resilience proposed the description of these individuals as resilient agers<sup>[5]</sup>, cognitively elite<sup>[6]</sup>, optimal memory performers<sup>[7]</sup>, using validated psychometric criteria. In an original study, Harrison et al.<sup>[3]</sup> demonstrated that HPOAs did not have significant cortical atrophy and presented thickening of the anterior cingulate cortex compared to the individuals in the control group.

The term HPOAs, first mentioned by Cabeza<sup>[8]</sup> and indicated by Borelli et al.<sup>[2]</sup>, promotes an expanded concept, which may vary according to local cultural and sociodemographic characteristics. Additionally, they may have biological, neurocognitive and image aspects that can differentiate them from other NOAs, providing resilient brain structure<sup>[9]</sup>.

Neuropsychological models indicate that cognitive decline is a consequence of aging, becoming more pronounced after the sixth decade of life in Neurotypical Older Adults (NOAs)<sup>[10,11]</sup>. However, there is variability in cognitive trajectories, and it increases with age, indicating that individual differences grow with advancing age<sup>[12]</sup>. Some of these differences have been explained by effects, such as preclinical neurodegenerative disease, Alzheimer's disease in samples of older individuals<sup>[13]</sup>, as well as the presence of NOAs or HPOAs.

Some proposed cognitive theories, such as cognitive reserve and brain maintenance<sup>[14,15]</sup>, have sought to explain the variability in cognitive trajectories, with some older individuals starting to decline earlier and others maintaining their independence and well-being. Studies in neurosciences and neuroimaging have led to advances in understanding the neural mechanisms related to cognitive

outcomes already described by Cabeza et al.<sup>[16]</sup>, who proposed the contribution of reserve, maintenance, and compensation mechanisms in the individual variability of cognitive trajectories.

In Brazil, given the variability of the educational and socio-cultural profile of the older population, studies are needed to document the profile of these HPOAs, as well as the effectiveness of interventions that promote cognitive health. The objective of the research is to investigate the associations between cognitive, physical, and psychological measures in NOAs and HPOAs and their relationship with physical and psychological measures, as well as to characterize the profile of HPOAs in psychological and physical measures.

## 2. Materials and Methods

This is a quantitative, exploratory, and quasi experimental study that used a longitudinal design, being approved, as well as its Informed Consent Form, by the Research Ethics Committee of the university, *Certificado de Apresentação para Apreciação Ética* (CAAE, Presentation Certificate for Ethical Appreciation) number *information suppressed for evaluation* and opinion number *information suppressed for evaluation*. Data collection was performed between June 2017 and July 2018.

### Sample

The convenience sample consisted of 27 older adults with a mean age of 71 years ( $SD = \pm 3.59$ ) from the (*information suppressed for evaluation*) group. In the sample, 21 were characterized as NOAs and six as HPOAs. The study started with the participation of 85 individuals and continued with 51 individuals, after the baseline assessment, from which they were distributed in mnemonic strategies (MEMO) or cognitive stimulation (*Stimulus*), and again distributed to a physical training program (aerobic training associated with a systematic and personalized exercise program) or psychoeducational intervention (health education lectures). A total of 17 participants made up the sample loss after one year, and seven did not participate in any of the assessments. We allocated the participants so that they could be compared to a memory intervention group and a physical training or psychoeducational intervention program.

### Instruments

In addition to the Anamnesis, composed of sociodemographic, health and lifestyle data, participants were assessed by physical, psychological, and cognitive measures, detailed below:

Physical measures: a) the muscle strength control test (handgrip strength), respecting the criteria described by Shiratori et al. <sup>[17]</sup>, three attempts alternating the limbs, with an interval of 60 seconds and being instructed to the maximum isometric contraction after the verbal command; b) the cardiorespiratory capacity test (CRC) with continuous monitoring of the electrocardiogram, added to serial blood pressure measurements, in order to determine V02 max; c) the Dual Energy X-ray Absorptiometry body composition measure to quantify lean mass, fat mass and bone component (DPX-L) with full body assessment, using the LUNAR software, v1.2, for this analysis.

Psychological measures: a) the questionnaire of the World Health Organization Quality of Life Group (WHOQOL-OLD), according to Fleck et al. <sup>[18]</sup>, b) the Beck Anxiety Inventory (BAI) to measure levels of anxiety, according to the guidelines of Beck and Steer <sup>[19]</sup>, c) the 15-item Geriatric Depression Scale (GDS) adapted for the Brazilian population by Almeida and Almeida <sup>[20]</sup>.

Cognitive measures: a) the Addenbrooke Cognitive Exam – Revised. The ACE-R is used to assess five cognitive domains, offering a total and partial score for each domain, adapted and validated for Brazil as a cognitive screening test by Carvalho and Caramelli <sup>[21]</sup>; b) the Rey Auditory-Verbal Learning Test - Using the adapted version of the RAVLT for the older population of Brazil <sup>[22]</sup>; c) the Victoria Stroop Test <sup>[23]</sup>.

### Methodological procedures

In the present study, data referring to 12 months of follow-up will be presented, including four stages: 1) selection and recruitment, 2) assessment 1 (baseline), 3) assessment 2 (six months later) and 4) assessment 3 (one year later).

For Assessment 1, all participants were assessed individually through Anamnesis and psychological, physical, and cognitive measures. For each of these steps, a researcher was responsible for the respective area with the help of assistants, and each assessment lasted about 60 minutes.

Assessments 2 and 3 followed the same procedures as in Assessment 1, with a six-month period for each assessment. In the first six months, the participants were subdivided into two groups of cognitive interventions consisting of eight weekly sessions: training based on mnemonic strategies (MEMO) or the cognitive stimulation program (*Stimullus*). The *Stimullus* program sessions comprised cognitive stimulation activities, based on the discrimination of visual and auditory stimuli, and the MEMO program sessions focused on the use and training of mnemonic strategies of categorization, the

place association method, verbal association, and reading method, according Chariglione, Janczura e Belleville <sup>[24]</sup>.

Subsequently, for the next six months, the participants were divided according to age, sex, and educational level in two groups with the following activities: a physical training program (aerobic training associated with a systematic and personalized workout program) or a psychopedagogical health intervention, based on 60-to-90-minute lectures with topics related to the well-being and health in aging.

### Data analysis

Initially, the descriptive data of the sample were analyzed by mean, standard deviation and frequencies. Normality was tested for all variables, investigated by the Shapiro-Wilk test. As most of the data did not follow a normal distribution, the analyzes were performed using the non-parametric statistical Mann-Whitney tests, to compare the performance of the groups, and the Wilcoxon test, to compare the effects of the interventions comparing the initial performance to the assessment performed after six months and one year. The R software, version 3.4.3, and the SPSS software, version 20, were used for the analyzes - both with a significance level of  $p \leq 0.05$ .

## 3. Results

### Descriptive analysis

An analysis of sociodemographic variables showed 23 older women (85.19%) and 04 older men (14.81%), with a higher frequency of individuals aged from 67 to 72 years (N = 16; 59.26%), followed by individuals from 61 to 66 (N=5; 18.52%), and 73 to 78 years (N = 5; 18.52%) for each interval, with only one individual (3.70%) aged between 79 and 84 years. As for their educational level, the individuals were evenly distributed in the groups ranging from incomplete elementary education and complete higher education. Regarding marital status, 11 were married (40.74%), 2 were single (7.41%), 6 were separated/divorced (22.22%), 1 was widowed (3.70%) and 7 were in the “others” category (25.93%).

Physical, psychological, and cognitive measures of the sample are shown in Table 1. The participants' handgrip strength of the dominant hand average was 24.11 Kgf/cm<sup>2</sup> (SD = ± 6.52). According to Shephard's criteria <sup>[25]</sup>, handgrip strength at 55 years old is 34 Kgf/cm<sup>2</sup> and that, at 75 years old, it drops to 22 Kgf/cm<sup>2</sup>, and that the handgrip strength measures of these individuals are directly proportional to their overall muscular strength. Regarding body composition, most of the sample was overweight (BMI greater than 25.8kg/m<sup>2</sup> and with fat mass of 35.4%).

Regarding bone mineral density, the average obtained was 1.128 kg (SD = ± 102). The minimum value between the predicted and assessed maximum oxygen consumption (VO<sub>2</sub>max) levels was 48% with an average of 82%. The maximum value was 29.41 ml.kg.min. The VO<sub>2</sub>max/PV ratio had the following results: 20 ml/pulse (maximum) and 6.5 ml/pulse (minimum).

According to Table 1, the domains of WHOQOL OLD (such as sensory functions, death, and dying) had a mean lower than 3.5 (2.35 and 2.17), respectively. Regarding the presence of symptoms of anxiety and depression, the sample scores demonstrated low levels of anxiety and/or depression (BAI: 4.52 SD = ± 4.24; GDS: 2.59 SD = ± 2.15). In cognitive measures, such as Stroop (time), 75%

**Table 1.** Description of the Physical, Psychological and Cognitive Variables (N=27), Brasília, DF, 2019.

Variable	Min	1stQ	Med	Mean	3rdQ	Max	SD
<b>Physical measures</b>							
Handgrip strength of the dominant hand (Kgf/cm <sup>2</sup> )	14.00	19.00	25.00	24.11	29.00	38.00	6.52
Cardiorespiratory Capacity (ml/kg/min)	48%	64%	81%	82%	97%	136%	22%
DMO (gl/cm <sup>2</sup> )	962	1048	1112	1128	1188	1311	102
DXA (%G)	14.90	32.10	36.70	35.40	40.50	53.30	8.69
Fat mass (Kg)	9.30	19.20	23.80	25.20	31.20	56.90	9.98
Lean mass (Kg)	30.30	38.50	42.90	44.60	48.70	65.40	8.17
BMI (Kg/m <sup>2</sup> )	21.20	25.80	28.00	28.90	31.70	45.40	5.11
<b>Psychological measures</b>							
Whoqol old - Sensory Functions	1.75	2.00	2.25	2.35	2.50	3.50	0.46
Whoqol old - Autonomy	2.75	3.38	3.50	3.70	4.00	4.75	0.51
Whoqol old - Past, present and future activities	2.75	3.50	3.75	3.90	4.25	5.00	0.60
Whoqol old - Social Participation	2.75	3.50	3.75	3.90	4.25	5.00	0.60
Whoqol old - Death and dying	1.0	1.75	2.00	2.17	2.38	4.00	0.73
Whoqol old - Intimacy	1.0	3.25	3.50	3.46	4.00	4.75	0.94
Beck's anxiety inventory	0.00	1.00	3.00	4.52	7.00	16.00	4.24
Geriatric Depression Scale	1.00	1.00	2.00	2.59	3.50	8.00	2.15
<b>Cognitive measures</b>							
Stroop (time)	13.00	23.80	27.00	28.00	31.70	61.30	8.52
ACE-R	44.00	73.00	80.00	78.26	89.50	96.00	13.49
ACE-A	11.00	14.00	17.00	15.60	17.50	18.00	2.24
ACE-M	10.00	14.50	19.00	18.60	23.00	26.00	4.96
ACE-F	3.00	8.00	10.00	9.44	11.00	13.00	2.74
ACE-L	9.00	20.50	24.00	22.00	25.00	26.00	4.10
ACE-V	8.00	12.00	14.00	13.20	15.50	16.00	2.65
Learning curve (RAVLT)	26.00	34.50	41.00	42.50	48.00	71.00	10.70
Forgetting speed (RAVLT)	0.78	0.93	1.00	1.09	1.13	2.50	0.32
Proactive interference (RAVLT)	0.20	0.67	0.80	0.84	1.00	1.75	0.35
Retroactive interference (RAVLT)	0.29	0.71	0.80	0.78	0.88	1.00	0.18

Note: ACE-R = Addenbrooke's Cognitive Examination – Revised; ACE-A = Attention and orientation, ACE-M= Memory; ACE-F = Fluency; ACE-L = Language; ACE-V = Visuospatial; RAVLT = Rey Auditory Verbal Learning Test Learning; Min= Minimum; 1<sup>st</sup>Q = 1<sup>st</sup> Quartile; Med = Median, 3<sup>rd</sup>Q = 3<sup>rd</sup> Quartile; Max = Maximum; SD = Standard Deviation.

of individuals taking less than or equal to 31.70 seconds. On the ACE-R, memory test was the domain with the greatest variability.

Among the assessments that make up the Rey Auditory-Verbal Learning Test (RAVLT), namely, learning curve, forgetting speed, proactive interference (PI) and retroactive interference (RI) indices, the mean values were, respectively, 48, 1.13, 1 and 0.88. The learning curve showed a relatively high SD (10.70) and the proactive and retroactive interference indices had mean values equal to 0.8.

**Classification of high-performing older adults**

Individuals were classified as HPOAs using their performance in the RAVLT - Learning Curve (sum of A1 to A5) <sup>[22]</sup>. According to the positive correlation (Spearman’s Correlation Coefficient: 0.604, p = 0.001) between educational level and the performance in the RAVLT - Learning Curve (A1-A5), we chose to consider the mnemonic performance according to the educational level. Thus, to compose the HPOA group, a performance higher than the 75th percentile on the RAVLT Learning Curve at baseline (first assessment) was considered for the groups ranging from “Incomplete Elementary School and Incomplete High School” or 5 to 10 years (>34 points) of education, and “Complete High School to Higher Education” or 11 years or over of education (> 50 points)

(refer to Table 2). Based on this criterion, six individuals were classified as HPOAs, three of whom having between 5 and 10 years of education, and three having 11 years or over.

**Neurotypical Older Adults vs. High Performing Older Adults**

As shown in Table 3, there were statistically significant differences between the group of individuals with typical performance and the HPOA group at baseline regarding their performance in the RAVLT (Recovery 1 to Recovery 5, and Recovery 7) and number of depressive symptoms, indicating that the HPOA group had a superior memory performance and a lower prevalence of depressive symptoms than the NOA group. There were no differences between groups regarding age, ACE-R performance, Stroop and WHOQOL-OLD scores.

Regarding physical performance measures, for the purposes of homogenization, we excluded four older men who composed the NOA group and, thus, the analyzes were carried out with 17 older women in the typical group and six older women in the HPOA group. As shown in Table 4, at baseline, the groups were similar in terms of body composition and physical fitness. However, there is a tendency for the group with better mnemonic performance to present lower waist circumference (p=0.06).

**Table 2.** Score on the Rey Auditory Verbal Learning Test Learning Curve according to the educational level and classification of High Performing Older Adults (N=27), Brasília, DF, 2019.

	N	Mean	SD	Med	Min	Max	P-25	P-75
General sample (N=27)								
5 to 10 years	13	31,77	9,66	32,00	17	48	25	34
11 years or over	14	40,71	8,77	38,50	27	55	36	50
5 to 10 years (N=13)								
Neurotypical older adults	10	27,70	6,53	30,50	17	34	23	33
High-cognitive performing older adults								
11 years or over (N=14)	3	45,33	3,06	46,00	42	48	42	48
11 years or over (N=14)								
Neurotypical older adults	11	37,18	5,95	37,00	27	50	35	40
High-cognitive performing older adults								
	3	53,67	1,53	54,00	52	55	52	55

Note: N = Number of subjects; SD = Standard Deviation; Min= Minimum; Max =Maximum; P-25= Percentile 25; P-75= Percentile 75.

**Table 3.** Cognitive and psychological performance in Neurotypical Older Adults and in High Performing Older Adults (N=27), Brasília, DF, 2019.

		Neurotypical Older Adults (N=21)		High Performing Older Adults (N=6)		P value
		Mean	SD	Mean	SD	
Age		70.19	5.48	69.83	3.60	0.93
SEX	Female	N=17	81%	N=6	100.0%	0.54
	Male	N=4	19%	N=0	0.0%	
STROOP_TIME	STROOP 1	25.24	11.81	19.67	5.65	0.26
	STROOP_ERROR 1	1.71	1.93	1.50	1.38	0.89
STROOP_TIME	STROOP 2	29.62	7.07	27.17	10.21	0.19
	STROOP_ERROR 2	3.14	3.69	1.83	1.33	0.71
STROOP_TIME	STROOP 3	46.29	34.38	34.83	8.08	0.32
	STROOP_ERROR 3	5.48	3.66	4.50	3.89	0.51
STROOP_INTERFERENCE		21.05	26.19	15.17	7.73	0.63
	RAVLT_A1	3.43	1.40	6.17	2.93	<b>0.02*</b>
	RAVLT_A2	6.19	1.72	9.00	1.41	<b>0.00*</b>
	RAVLT_A3	7.19	1.97	10.83	.75	<b>0.00*</b>
	RAVLT_A4	7.62	1.96	11.83	.75	<b>0.00*</b>
	RAVLT_A5	8.24	2.34	11.67	1.37	<b>0.00*</b>
	RAVLT_A6	5.57	2.58	8.67	3.50	0.06
	RAVLT_A7	5.48	2.27	9.33	2.16	<b>0.00*</b>
	RAVLT_RECOGNITION	12.19	2.06	13.33	2.73	<b>0.01*</b>
	RAVLT_V_FORGETTING	1.19	.75	1.33	.52	0.50
	PI	1.29	.96	.83	.41	0.29
	RI	.71	.46	.67	.52	0.89
	ACE-A	15.24	2.64	15.50	2.35	0.89
	ACE-M	15.95	5.83	18.67	5.61	0.41
	ACE-F	8.90	3.25	10.50	1.22	0.24
	ACE-L	20.10	4.90	24.00	2.37	0.12
	ACE-V	12.62	2.44	13.83	2.40	0.24
	ACE-R	72.81	14.70	82.50	10.60	0.14
	MMSE	24.10	3.70	26.17	2.79	0.22
	GDS	3.33	2.27	2.17	1.72	<b>0.01*</b>
Whoqol old - Sensory Functions		9.81	2.64	9.33	2.80	0.72
Whoqol old - Autonomy		14.05	2.52	15.67	2.16	0.24
Whoqol old - Past, present and future activities		15.19	2.73	16.00	2.19	0.41
Whoqol old - Social Participation		15.19	2.84	15.33	3.01	1.00
Whoqol old - Death and dying		10.24	4.28	7.33	2.25	0.08
Whoqol old - Intimacy		15.00	3.89	16.17	2.32	0.55
Whoqol old - overall		79.48	11.12	79.83	8.42	1.00

Note: N = Number of subjects; SD = Standard Deviation; RAVLT= Rey Auditory-Verbal Learning Test; RAVLT\_REC = Forgetting speed; PI= proactive interference index; RI= retroactive interference index; MMSE = Mini Mental State Examination; GDS = Geriatric Depression Scale; \*p≤0,01.



**Table 4.** Anthropometric and physical fitness variables among Neurotypical Older Adults and High Performing Older Adults (N=27), Brasília, DF, 2019.

	Neurotypical Older Adults (N=17)		High Performing Older Adults (N=6)		P value
	Mean	SD	Mean	SD	
Weight (Kg)	70.88	10.87	71.33	23.36	0.47
Height (m)	1.94	.24	2.00	.00	0.86
BMI	28.53	3.62	29.33	10.17	0.35
RSP	128.00	21.65	127.33	23.65	0.92
RDP	74.47	9.45	74.17	8.47	0.92
Bpm	77.12	13.01	77.33	7.61	1.00
Waist circumference	97.65	6.65	93.17	14.80	0.06
Hip circumference	104.29	7.86	106.83	18.54	0.61
DHM (Pounds/F)	41956.76	5857.87	42758.17	6346.88	0.47
NDHM (Pounds/F)	44.53	9.96	44.83	7.99	1.00
BMD g/cm <sup>2</sup>	922.41	445.30	1124.83	67.60	0.47
DEXA (%G)	38.82	5.05	34.67	12.29	0.61
VO <sup>2</sup> ml/kg.min	19.65	4.36	19.83	5.34	0.29
HR max (bpm)	135.71	21.09	142.67	13.09	0.71
VO <sup>2</sup> /FC max (ml/b)	10.35	2.83	9.17	1.17	0.81
PV max (l/min)	51.47	15.46	44.17	13.41	0.23

Note: SD = Standard Deviation; BMI= Body Mass Index; RSP= Resting systolic pressure. RDP= Resting diastolic pressure. Bpm= Beats per minute. DHM= Dominant Hand Mean. NDHM= Non-Dominant Hand Mean. BMD= Bone mineral density; DEXA= Dual-energy X-ray absorptiometry bone mineral density; VO<sub>2</sub>max = maximum oxygen consumption; HR=Heart rate; PV= Pulmonary ventilation.

### Follow-up

Regarding the follow-up assessment (after six months and one year), we observed that NOAs had a higher performance in the ACE-R Total in the assessment performed after six months and a reduction in the number of depressive symptoms after one year, when compared to the number of depressive symptoms in the initial assessment. In the assessment performed after one year, they were also slower in the Stroop test condition 3.

As for the parameters of physical fitness, this group also showed an increase in Bone Mineral Density in their subsequent assessments, and variation in their DEXA,

with an increase in fat mass in the assessment performed after six months and a reduction in the assessment performed after one year, which may be associated with type of intervention to which they were engaged: in the first semester they performed only cognitive interventions and, in the second semester, part of this group performed physical stimulation activities (resistance and aerobic training). According to Table 5, the same changes were not observed in the HPOA group, however it is necessary to consider that the reduced number of participants may have reduced the statistical power of the analyzes. The general sample had similar gains to the typical performance group.

**Table 5.** Follow-up measures in multimodal interventions in Neurotypical Older Adults, High Performing Older Adults, highly cognitive older adults, and general sample (N=27), Brasília, DF, 2019.

	Neurotypical Older Adults (N=21)			High Performing Older Adults (N=6)			General sample (N=27)		
	Mean	SD	P	Mean	SD	P	Mean	SD	P
<b>RAVLT_IP</b>									
IA	1.28	.95		.83	.40		1.18	0.87	
6M	1.00	.63	0.29	.83	.40	0.75	0.96	0.58	0.26
1Y	.95	.38	0.19	.66	.51	0.50	0.88	0.42	0.12
<b>ACE_R</b>									
IA	72.80	14.70		82.50	10.59		74.96	14.30	
6M	76.38	15.44	<b>0.04</b>	81.16	15.48	0.94	77.44	15.28	0.09
1Y	76.80	13.02	0.05	83.33	15.12	0.62	78.25	13.49	<b>0.04</b>
<b>S_T3</b>									
IA	46.28	34.38		34.83	8.08		43.74	30.75	
6M	42.30	24.63	0.33	36.66	14.90	0.92	41.11	22.70	0.34
1Y	36.65	13.94	<b>0.01</b>	34.33	10.55	0.49	36.29	13.12	<b>0.01</b>
<b>GDS</b>									
IA	4.04	2.31		1.66	1.21		3.51	2.32	
6M	3.33	2.26	0.15	2.16	1.72	1.00	3.07	2.18	0.24
1Y	3.04	2.24	<b>0.02</b>	1.00	.00	0.37	2.59	2.15	<b>0.01</b>
<b>OQL</b>									
IA	79.47	11.12		79.83	8.42		79.55	10.43	
6M	80.80	10.44	0.46	81.16	4.35	0.65	80.88	9.36	0.37
1Y	76.80	5.82	0.29	80.50	4.72	0.87	77.62	5.73	0.42
<b>WC</b>									
IA	99.61	8.08		93.16	14.79		98.18	9.99	
6M	99.90	7.75	0.56	95.66	16.48	0.25	98.96	10.08	0.28
1Y	100.00	9.07	0.35	98.50	19.48	0.12	99.66	11.69	0.42
<b>BMD(g/cm<sup>2</sup>)</b>									
IA	978.38	416.85		1124.83	67.60		1010.92	372.018	
6M	1105.15	105.24	0.36	1135.66	69.34	0.44	1112.19	97.73	1.00
1Y	1127.04	106.94	<b>0.01</b>	1131.00	88.99	1.00	1127.92	101.60	<b>0.04</b>
<b>DEXA(%G)</b>									
IA	37.09	6.45		34.66	12.29		36.55	7.88	
6M	42.80	9.07	<b>0.00</b>	39.33	17.00	0.12	42	11.07	<b>0.00</b>
1Y	35.57	7.74	<b>0.03</b>	35.00	12.37	0.81	35.44	8.69	0.08

Note: SD = Standard Deviation; P= P Value; IA= Initial assessment; 6M= 6 months; 1Y= 1 year; RAVLT\_IP = proactive interference index; S\_T3= Stroop\_Time3; GDS= Geriatric depression scale; OQL= Overall quality of life; WC= Waist circumference; BMD= Bone mineral density; DEXA= Dual-energy X-ray absorptiometry bone mineral density.



## 4. Discussion

In the present study, HPOAs had a lower prevalence of depressive symptoms than NOAs at baseline and there were gains in global cognitive performance, mood, and physical fitness variables associated with multimodal interventions, evident in the NOA group. Thus, the NOA group presents higher benefits than the HPOA one, but it could be tested in the next studies due to our reduced sample.

In this study's sample, we observed that the HPOA group was composed by six older women. Previous studies indicated that higher prevalence of HPOAs was observed in women than in men<sup>[26]</sup>. Maccora et al.<sup>[27]</sup> observed a higher prevalence of female HPOAs (85.19%) and no association between most factors previously associated with cognitive decline. For women, the associated factors were a higher number of years of education and a higher frequency of investigative activities. Modern studies corroborate the role of educational level in the cognitive and cerebral reserve and the association of years of education with a higher-than-average episodic memory<sup>[28]</sup>.

Regarding physical aspects, specifically muscle strength, the results presented here coincide with previous studies<sup>[29,30]</sup> and demonstrate that the average muscle strength is above the cutoff point in relation to what is necessary for daily life activities. About cardiovascular performance, as demonstrated by other authors<sup>[31,32]</sup>, this may be associated with a reduction in the risk of cognitive decline in older individuals. Stability of cardiorespiratory capacity was observed in relation to the follow-up period.

However, physical measures did not differ between HPOAs and NOAs. Only waist circumference had statistical significance, with lower circumferences in the HPOA group than in the NOA group at baseline. Concerning the psychological variables, the presence of above-average values in aspects related to quality of life (WHOQOL-OLD) and the absence or low levels of anxiety and/or depression (BAI and GDS) stands out. The results of a number of studies suggest that some mechanisms could be involved in this correlation, such as the association of depression and anxiety with high levels of glucocorticoids and subsequent neuronal damage, as well as greater activation of the limbic system to the detriment of cortical areas<sup>[34]</sup>.

As for cognitive aspects, the results obtained in the ACE-R are like those described by Carvalho and Caramelli<sup>[21]</sup>. Regarding the RAVLT scores, which assesses recent memory, learning, interference, and recognition memory, as expected, a better performance was observed in the HPOA group. Nitrini et al.<sup>[35]</sup> studied

the influence of age and education in neuropsychological tests and observed differences in memory performance, considering literate and illiterate individuals. Regarding the Stroop test, which assesses attention and executive functions, the results related to the measurement of time indicated an average value of 28s, with the minimum and maximum values being 13 and 61.3, respectively.

In summary, the data on stability and increase in cognitive functions over time, when analyzed longitudinally, have implications in the context of aging and in the HPOA study, with the prospect of a successful aging necessarily linked to cognition.

Although the findings are promising, this is an exploratory study, in which we intended to verify differences and the trajectory of HPOAs and NOAs in physical, cognitive, and psychological measures after participating in multimodal interventions. A high research dropout rate out of 50% of the sample, and this could be associated with the number of assessments and interventions. In addition, the small sample (HPOA group n=6; NOA group n=21) did not allow us to perform multiple comparisons and more sophisticated statistical analysis. Due to these limitations, these findings could not be generalized, and other studies need to test the efficacy of each intervention.

## 5. Conclusions

A higher mnemonic performance in older adults was associated with emotional health variables, while multimodal interventions proved to be beneficial in the context of Brazilians older adults. This is a new branch of research in Gerontology and neurosciences and the cooperation of different research programs is necessary to understand the impact of multimodal interventions in different cognitive profiles.

## Author Contributions

Alessandro Amorim AITA - Investigation (Lead), Conceptualization (Lead), Formal analysis (Equal), Project administration (Equal), Writing-original draft (Equal), Writing-review & editing (Equal).

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## Conflict of Interest

The authors report no conflicts of interest.

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