No evidence of reduced capacity during highly demanding cognitive tasks in healthy older adults at electroencephalographic risk of cognitive impairment

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Abstract

Healthy older adults with excessive theta absolute power (AP) are considered at electroencephalographic risk of developing cognitive impairment 7 to 10 years later. Although this population may exhibit a normotypic cognitive state, as revealed by traditional neuropsychological assessment, less is known about their performance during tasks with high cognitive demand and whether the degree of excessive theta AP can be used to predict their performance, which was our objective. We compared the scores from highly demanding memory tasks (i.e., the Visual Short-Term Memory Binding Test (VSTMBT) and the Loewenstein-Acevedo Scale for Semantic Interference and Learning (LASSI-II)) between older adults with and without excessive theta AP. No significant differences were found between the groups for any test score or for the predictive value of theta AP for performance. The results of this study provide evidence that older adults with excessive theta AP do not exhibit impaired performance in highly demanding cognitive contexts. The possible role of cognitive reserve in alleviating evidence of deterioration is discussed.

Keywords: Cognitive decline, EEG, neuropsychological assessment, older adults, theta.

Introduction

As a result of population growth and aging, the World Health Organization estimates that, by 2030, the number of adults over 60 will reach 65.7 million people worldwide [1]. In Mexico, it is estimated that this number will reach 20 million [2]. Advanced age is the main risk factor for the development of neurocognitive disorders [1], which in severe cases result in disability and dependence, causing heavy emotional and economic costs at the individual, family, and social levels [3]. There is an increasing need to identify biomarkers capable of detecting the first physiological correlates of pathological cognitive aging before the onset of a neurocognitive disorder. Currently known biomarkers with the capacity to detect subtle changes include the concentrations of amyloid beta (Aβ42) and tau proteins in cerebrospinal fluid (CSF) and amyloid positron emission tomography features [4]. These biomarkers are invasive and expensive; therefore, there is a need to identify non-invasive and cost-effective measures sensitive to early subtle brain changes that occur in the preclinical phase of a neurocognitive disorder.

From a neurophysiological perspective, the resting-state electroencephalogram (EEG), which reflects the functional integrity of the brain, has been established as a sensitive neuroimaging technique to detect incipient changes in neural activity in the early stages of a neurocognitive disorder [5,6]. Prichep et al. [7] reported that healthy older adults with subjective memory complaints (Global Deterioration Scale=2) and excessive absolute power (AP) in the theta frequency band had an increased risk of developing major cognitive impairment 7 to 10 years later. In addition, excessive theta power in older adults has been associated with increased Aβ deposition in the brain [8], decreased concentrations in CSF [9], decreased brain and hippocampal volumes [10], and progressive subjective cognitive decline [11]. Our research group studied this

electroencephalographic risk marker in healthy older adults and identified EEG changes in both functional connectivity at rest [12] and event-related potentials during cognitive tasks [13,14]. In those studies, we did not find behavioral differences associated with high theta power, probably due to the use of traditional neuropsychological tests. However, Prichep et al. [7] reported that older adults who later exhibited cognitive deterioration and had higher theta AP also performed worse on attention tests, i.e., the Digit Span Test (forward and backward) and the Digit Symbol Substitution Test.

In addition to these neurophysiological approaches, efforts have been made to develop new neuropsychological tests that are capable of detecting subtle changes in cognitive processes during the preclinical phases of neurocognitive disorders [15,16,17,18,19], that is, when individuals report subjective cognitive decline that is not psychometrically objective and therefore does not meet the criteria for a neurocognitive diagnosis [20]. This effort has arisen because traditional neuropsychological tests have been shown to lack sensitivity for detecting subtle cognitive decline [19,21]. Recent evidence suggests that tasks with high cognitive demand, due to either interference control requirements or working memory load, may be sensitive to early cognitive changes in preclinical Alzheimer's disease [18]. Specifically, Parra et al. [21] reported that asymptomatic carriers of the E280A0 mutation of the presenilin 1 gene (familial Alzheimer's disease) performed worse than healthy adult controls did in the Visual Short-Term Memory Binding Test (VSTMBT), a visual working memory test with varying levels of perceptual load demand. Koppara et al. [22] also reported worse performance in the feature binding task (short-term memory binding condition) of the VSTMBT in subjects with cognitive complaints. In both studies, no differences were found between groups in other neuropsychological tests.

Similarly, Loewenstein et al. [18] reported significantly lower performance in older adults with subjective cognitive complaints (pre-mild cognitive impairment [PreMCI]) than in controls using the Loewenstein-Acevedo Scale for Semantic Interference (LASSI), a verbal memory test requiring effective proactive and retroactive interference control. Additionally, Crocco et al. [16] reported that the percentage of semantic intrusions in this test distinguished subjects with PreMCI from controls. Loewenstein et al. [18] reported an association between increased Aβ load on positron emission tomography (PET) brain scans and failure to recover from proactive semantic interference as measured with the LASSI in otherwise neuropsychologically normal older adults. Using this test, they also found an association among brain volume loss [23], hippocampal and precuneus cortical thinning [24], and failure to recover from proactive semantic interference in participants with early amnestic MCI.

Our study breaks new ground in this field by investigating the potential relationship between EEG-based biomarkers of cognitive impairment risk and neuropsychological tests that have demonstrated high sensitivity to the preclinical phases of neurocognitive disorders. This study aimed to fill a significant gap in the current literature. Our research goal was to determine whether there are discernible alterations in scores on highly demanding cognitive tests (i.e., the VSTMBT and LASSI-II) in healthy older adults with electroencephalographic risk of cognitive impairment (excessive theta AP) and whether the degree of theta AP predicts their performance.

Materials and methods

The present study was approved by the Bioethics Committee of the Institute of Neurobiology (INB) at Universidad Nacional Autónoma de México (UNAM, REF 030-H-RM) in accordance with the guidelines established by the Declaration of Helsinki.

Participants

The sample included 63 healthy adults over 55 years of age with no history of neurological disease or current psychiatric diseases. The inclusion criteria were as follows: a) at least 9 years of formal education; b) normal global functioning (Global Deterioration Scale score $\leq$ 2; [24]); c) an age-adjusted normal cognitive state (Montreal Cognitive Assessment (MoCA) score > 23; [25-27]); d) average intelligence (Wechsler Intelligence Scale for Adults Version IV score > 80; [28]); e) normal daily functioning (Instrumental Activities of Daily Living Scale score < 8; [20,30]); and f) normal levels of hemoglobin, cholesterol, triglycerides, glucose, and thyroid-stimulating hormone. All participants were screened for psychopathology with the 5.0.0 Spanish version of the MINI International Neuropsychiatric Interview [31] and a semistructured clinical interview performed by a clinical psychologist and a neuropsychologist. Although some participants scored 1 standard deviation below their normative group on some neuropsychological tests, none of them met Jak and Bondi's criterion for a mild neurocognitive disorder of > 1 SD below the norm in two tests per cognitive domain [32]. Participants were recruited from the general population through social media advertisements, radio, and recommendations from other participants. All participants signed a letter of informed consent before starting any procedure.

Neuropsychological instruments

A neuropsychological battery of traditional tests was designed to explore memory (Rey's complex figure [RCF], logical memory, and verbal paired associates [PAs]), executive functioning (phonological and semantic verbal fluency, mazes, Tower of Hanoi [3- and 4- disc versions], Trail Making Test [TMT] A and B, and Stroop), and intellectual capacity (WAIS-IV; [28]). Tests were selected from the Neuropsi Attention and Memory battery (NAM-2; [33]), the Neuropsychological Battery of Executive Functions and Frontal Lobes (BANFE- 2; [34]), and the versions of the TMT by Arango-Lasprilla et al. [35] and Stroop de Rivera et al. [36]. In addition, the VSTMBT [37] and the Loewenstein-Acevedo Scale for Semantic Interference and Learning II (LASSI-II; [18]; Roa et al., in preparation) were administered. The VSTMBT consists of a visual short-term memory task with two conditions: one requires the individual to remember the shape (single condition) of geometric stimuli, and the other requires them to remember both the color and the shape (binding condition). Both visual versions had low cognitive load (remember two forms) and a high cognitive load (remember three forms) forms and were presented interleaved (Fig 1). The percentage of correct responses was used for the analysis. After a warning stimulus (+), the figure to be remembered was presented for 2 s (encoding phase). A blank screen was presented for 1 s (retention phase), and finally, a second figure (probe) was presented. The participant reported verbally whether the encoding and probe figures matched. As soon as the participant gave an answer, the researcher presented the next trial. A total of 32 trials were performed for each condition.

Please, insert Figure 1

Figure 1. **Example of two VSTMBT items with high cognitive load**. The upper row shows a single-condition trial (shape). The lower row shows a binding-condition trial (shape and color). “+” is the fixation visual point. Adapted from [38].

The LASSI-II is a word learning test that requires individuals to learn 2 lists (i.e., A and B) of 15 words each, which contain three semantic categories: 5 fruits, 5 clothes, and 5 musical instruments. This test involves a free recall (free recall A and B) and cued recall (cued recall A and B) after the first presentation of each list, a second learning trial for each list followed by a cued recall (cued recall A2 and cued recall B2), a free and cued recall of list A (free and cued recall A3) after cued recall B2 and a delayed recall of both lists. This test enables the assessment of maximum storage capacity (cued recall A2), the effects of proactive semantic interference (PSI) (cued recall B) and retroactive semantic interference (RSI) (cued recall A3), and recovery from PSI (r-PSI) (cued recall B2) after a second learning trial. The percentage of semantic intrusions was calculated for PSI and r-PSI, two measures that have been shown to be highly sensitive to cognitive decline. The percentage of PSI (% of intrusion errors on cued recall B) was calculated by dividing the total intrusions in cued recall B by the sum of total intrusions in cued recall B and total correct responses in cued recall B, and the percentage of r-PSI (% of intrusion errors on cued recall B2) was calculated by dividing the total intrusions in cued recall B2 by the sum of total intrusions in cued recall B2 and total correct responses in cued recall B2 (as in [16]). The total number of intrusions was calculated as the sum of all intrusions in the complete test. The tests were administered to all participants in the same order by a neuropsychologist.

The full neuropsychological battery was administered in the morning, and standardized scores were calculated for each measure using the corresponding norms for the Mexican population (except for the VSTMBT and LASSI-II, which do not yet have normative data).

EEG recording and analysis

A resting 19-channel EEG was recorded using the Medicid IV system (Neuronic Mexicana, SA, Mexico) and the Track Walker TM v2.0 data capture system. The electrodes were mounted on an elastic cap (Electro-Cap, International, Inc., Eaton, Ohio, USA) according to the International 10-20 System and referenced to linked earlobes. Recordings were carried out in a sound-muffled, air-conditioned, and faradized chamber with a comfortable chair and dim lighting. The participants were asked to keep their eyes closed, relax (without goal-directed purposeful thinking) and not fall asleep. The EEG acquisition lasted 10 minutes, with a sampling rate of 200 Hz, a gain of 20,000, and impedances below 10 kΩ.

The EEG was visually inspected with Track Walker TM v2.0 software by two electroencephalography experts, and 24 epochs of 2.56 seconds were selected manually. These epochs were free of physiological and non-physiological artifacts, as well as paroxysmal activity, and, in most participants, exhibited frequency and amplitude features of the posterior dominant alpha rhythm to avoid slow activity associated with drowsiness. Using Neuronic Quantitative Tomographic EEG software (Neuronic Mexicana S.A de C.V., version N_I_SW-5 6.2.4.0), the power spectrum was calculated from the selected epochs for each participant using fast Fourier transform with a spectral resolution of 0.39 Hz for each electrode and frequency bin (0.78–19.14 Hz). The spectral matrices were corrected by the global scale factor [39] to eliminate intrinsic non-neurophysiological interindividual differences. The AP was subsequently calculated at each electrode for the following frequency bands: delta [1.5–3.5 Hz], theta (3.5–7.5 Hz], alpha (7.5–12.5 Hz], and beta (12.5–19.5]. Z values for AP were subsequently obtained according to values from a normative database [40]. The participants were classified into two groups: i) the control group

(n=27), which consisted of participants with a normal EEG, i.e., without abnormal waveforms and a normal quantitative EEG in all frequency bands (-1.96 < z < 1.96), and ii) the risk group (n=36), which included participants with excessive theta AP (z > 1.96) in at least one electrode. Participants who exhibited any other abnormalities were excluded from the analysis.

To further study the relationship between excessive theta AP and cognition, the risk group was separated into two groups: the low-risk group (n=18) and the high-risk group (n=18). These groups were created by a median split according to four different criteria: the sum of the theta AP z value across all electrodes, the squared sum of the AP z value (maintaining the sign) across all electrodes, the mean of the theta AP z value across electrodes, and the number of electrodes with a theta AP z value > 1.96.

Statistical Analysis

A custom script for MATLAB R2020b (MathWorks, Natick, MA) was used for permutation statistical testing. The software Jasp 0.19.0 (https://jasp-stats.org) was used for the analysis of sociodemographic data, analysis of variance (ANOVA), principal component analysis (PCA), and regression analysis. All *p* values were corrected for multiple comparisons with the false discovery rate (FDR).

- *Risk group vs. control group*

Comparisons of cognitive measures and normalized AP values for each frequency band between groups were performed using the multivariate permutation method (5,000 permutations). This non-parametric technique does not assume an *a priori* theoretical distribution since the distribution of

null hypotheses of the statistical tests is generated iteratively through the random processing of the data. The probability values were corrected for multiple comparisons using the FDR. One subject was excluded from the group difference analyses involving AP because of data corruption in the EEG file.

For the analysis of continuous sociodemographic variables (age and years of schooling), the t test for independent samples was used. For the analysis of categorical variables (sex), the chi-square test (x^2) was used.

- High-risk group vs. low-risk group vs. control group

One-way ANOVA was used for the group comparisons between the control and low- and high-risk groups in the highly demanding cognitive tests.

- Multiple regression analysis between theta and cognition

Before the multiple regression analysis, a PCA of the theta AP z value of each electrode, using the varimax rotation method and a loading factor threshold of 0.7, was performed to identify the principal components (PCs) for use as predictors in the subsequent multiple regression analysis; the dependent variable was one cognitive score in each model. This analysis was performed to study the ability of excessive theta AP to predict performance on highly demanding memory tests and traditional neuropsychological tests.

Results

Demographic data

There were no significant differences between groups for age (risk: $\bar{x}$ = 65.55 +/- 7.45), control: $\bar{x}$ = 65.03 +/- 6.95), t = 0.28, *p* = 0.97), education (risk: $\bar{x}$ = 19.26 +/- 3.79), control: $\bar{x}$ = 20.37 +/- 4.36), t = -1.07, *p* = 0.97), or sex (risk female: 74.1%, control female: 69.4%; x^2 = 0.16, *p* = 0.97). In both groups, some individuals had scores below what was expected for their age on one of the traditional neuropsychological tests (control group: 44%, risk group: 47%), but they did not meet the criteria for a neurocognitive disorder [32].

EEG data

Our group formation criterion was based on theta AP according to age-adjusted norms. Therefore, there were statistically significant differences between the risk and control groups in the mean z theta AP at all electrodes (all *p* < 0.001; $\bar{x}$ = 7.33 +/- 2.76). Within the risk group, the electrodes with significantly higher theta zAP (z >1.96) were F8 (t = -5.33, *p* < 0.001), F4 (t = -4.99, *p* < 0.001), and P3 (t = 4.93, *p* < 0.001), whereas the control group had mean theta Z values close to 0 (Fig 2). There were no significant differences in the delta, alpha, or beta frequency bands.

Please insert Figure 2

Figure 2. **Z-based theta (3.5–7.5 Hz] AP in both groups**. a) Power spectra for the risk (red) and control (blue) groups (Pz as a representative electrode). b) Mean z theta absolute power topographic maps.

Cognitive results

- *Risk group vs. control group*

We did not find significant differences between the groups in any traditional neuropsychological test, including memory and executive function (Table 1) or intelligence tests (supporting information S1 Table).

Table 1. Traditional neuropsychological tests.

		Risk Mean(SD)	**Control** Mean(SD)	**t value**	***p*-FDR**
Memory	**RCF**				
	Copy	10.86(1.80)	9.77(2.10)	-2.14	0.65
	Retrieval	10.50(3.05)	9.92(2.09)	-0.84	0.96
	Logical memory				
	Encoding	13.77(2.84)	13.48(2.24)	-0.43	0.96
	Retrieval	11.91(2.63)	12.37(2.20)	-0.42	0.96
	PA				
	Encoding	11.16(2.62)	11.96(2.31)	1.21	0.89
	Retrieval	13.33(2.90)	13.03(2.20)	0.71	0.96
Executive	**Semantic fluency**	12.66(3.52)	12.51(3.09)	-0.19	0.97
	Phonologic fluency	14.05(3.25)	13.29(2.99)	-0.92	0.96
	Maze planning	11.30(2.14)	11.22(1.45)	-0.15	0.97
	Hanoi 3	11.16(2.06)	9.81(3.01)	-2.07	0.65
	Hanoi 4	8.16(3.73)	8.55(3.28)	0.43	0.96
	TMT-A	82.47(16.56)	79.70(20.05)	-0.59	0.96
	TMT-B	74.16(13.60)	69.37(14.79)	-1.32	0.87
	Stroop interference	42.58(19.37)	48.88(24.42)	1.15	0.90

RCF: Rey–Osterrieth complex figure; PA: verbal paired associates; TMT: Trail Making Test.

Similarly, we did not find significant differences between groups in any score of the VSTMBT (Table 2) or the LASSI-II test (Table 3), the total number of intrusions, the percentage of semantic intrusions (% of intrusion errors on cued recalls B and B2), or the recovery from interference (cued recall B2).

Table 2. Visual short-term memory binding test results in both groups.

VSTMBT	**Risk** Mean (SD)	**Control** Mean (SD)	**t value**	***p*-FDR**
STM Single 2	98.25(3.55)	96.51(6.57)	-1.33	0.87
STM Single 3	92.69(8.12)	87.01(19.29)	-1.06	0.94
STM Binding 2	91.99(9.03)	89.80(10.99)	-0.87	0.96
STM Binding 3	71.67(10.07)	75.67(13.35)	1.33	0.87

STM: short-term memory; 2: two objects to remember; 3: three objects to remember.

Table 3. Loewenstein–Acevedo Scale for Semantic Interference and Learning scores in both groups.

LASSI	Risk Mean (SD)	Control Mean (SD)	t value	*p*-FDR
Free recall A	10.27(2.66)	10.85(1.87)	0.94	0.96
Cued recall A	11.55(2.43)	12.14(1.48)	1.11	0.90
Cued recall A2 (maximum storage)	13.97(1.13)	14.40(0.63)	1.72	0.79
Free recall B	8.16(2.19)	8.11(2.02)	-0.13	0.98
Cued recall B (PSI)	8.22(2.49)	8.59(2.30)	0.58	0.96
Cued recall B2 (r-PSI)	1.91(1.88)	2(1.41)	0.14	0.97
Free recall A3	8.13(2.90)	8.59(2.62)	0.61	0.96
Cued recall A3 (RSI)	9.77(2.86)	10.11(3.40)	0.40	0.96
Delayed recall A and B	21.13(4.22)	21.66(4.11)	0.46	0.96
% of intrusion errors on cued recall B	0.14(0.11)	0.14(0.11)	-0.53	0.96
% of intrusion errors on cued recall B2	0.12(0.12)	0.14(0.10)	0.09	0.98
Total intrusions	1.48(1.54)	1.56(1.76)	0.44	0.96

PSI: proactive semantic interference; r-PSI: recovery from proactive semantic interference; RSI: retroactive semantic interference, A: first learning of the first list; A2: second learning of the first list with a cued recall; B: first learning of the second list; B2: second learning of the second list with a cued recall; A3: recall of the first list after interference of list B.

277 *- High-risk group vs. low-risk group vs. control group*

278 When three groups were considered (high risk, low risk, and control), for any of the four separation
279 criteria used, the one-way ANOVA used to compare the groups did not yield significant differences
280 in traditional neuropsychological test scores or highly demanding cognitive test scores (supporting
281 information S2-S5 Tables).

282 *- Regression analysis between the zAP (theta) value and cognition*

283 The principal component analysis of the *zAP (theta)* revealed three main components: PC1: frontal
284 component (F7, Fp1, Fp2, Fz, F3, F4, F8, and T3); PC2: centroparietal component (Pz, Cz, C4,
285 C3, P4, and P3); and PC3: occipitotemporal component (O1, O2, T6, and T5). No regression
286 model was statistically significant for any of the cognitive scores (Table 4).

287

288 **Table 4. Regression analysis results.**

Cognitive test	**R^2**	**F-Statistic** df(3,59)	***p*-FDR**
RCF			
Copy	0.04	1.01	0.96
Retrieval	0.03	0.61	0.96
Logical memory			
Encoding	0.02	0.39	0.96
Retrieval	0.009	0.18	0.97
PA			
Encoding	0.05	1.05	0.96
Retrieval	0.009	0.17	0.97

Semantic fluency	0.02	0.43	0.96
Phonologic fluency	0.12	2.78	0.65
Maze planning	0.08	1.71	0.87
Hanoi 3	0.05	1.11	0.96
Hanoi 4	0.07	1.48	0.89
TMT-A	0.02	0.50	0.96
TMT-B	0.02	0.58	0.96
Stroop interference	0.03	0.76	0.96
STM Single 2	0.31	0.63	0.96
STM Single 3	0.01	0.39	0.96
STM Binding 2	0.06	1.40	0.89
STM Binding 3	0.08	1.84	0.87
Free recall A	0.03	0.63	0.96
Cued recall A	0.01	0.31	0.97
Cued recall A2 (maximum storage)	0.07	1.55	0.89
Free recall B	0.03	0.68	0.96
Cued recall B (PSI)	0.02	0.42	0.96
Cued recall B2 (r-PSI)	0.01	0.38	0.96
Free recall A3	0.01	0.34	0.97
Cued recall A3	0.009	0.18	0.97

(RSI)			
Delayed recall	0.09	2.08	0.87
% of intrusion errors on cued recall B	0.001	0.01	1.00
% of intrusion errors on cued recall B2	0.003	0.06	1.00
Total intrusions	0.04	0.84	0.96

RCF: Rey–Osterrieth complex figure; PA: verbal paired associates; TMT: Trail Making Test; STM: short-term memory; r-PSI: recovery from proactive semantic interference; RSI: retroactive semantic interference.

Discussion

In this study, we aimed to explore potential cognitive differences between two groups: individuals with an EEG risk of cognitive impairment, defined by excessive theta activity, and control individuals with a normal EEG. Given the inability to identify cognitive differences between these groups using low-demand tests, our main objective, similar to that of previous studies [16,18,21,22], was to identify potential cognitive alterations in older adults in the presumably preclinical phase of a neurocognitive disorder using highly demanding tests (i.e., VSTMBT and LASSI-II) and traditional neuropsychological tests.

For the traditional neuropsychological tests, we did not find significant differences between the groups when separating a sample of healthy older adults according to their EEG (excessive theta or normal). The risk group did not differ from the control group, consistent with previous results [12, 13,14], despite separating the risk group according to severity (low risk, high risk) or looking for

relationships between theta activity and performance in these tests using multiple regression models.

Differences between the risk and control groups were expected when high cognitive demand tests were used; however, we did not detect any significant differences in the present study. Furthermore, we found no significant differences in highly demanding test results between the control group and the low- and high-risk groups. In addition, there was no association between theta activity and the LASSI-II and VSTMBT scores in the regression analysis. Notably, none of the previous studies [16,18,21,22] used the EEG as a group formation criterion but instead used clinical and neuropsychological criteria. To our knowledge, the study by Prichep et al. [7] is the only report exploring neuropsychological differences between older adults with and without electroencephalographic risk for cognitive decline that reported cognitive differences, specifically in the Digit Span and Digit Symbol Substitution tests. These contrasting findings might be because the participants in the study mentioned above, in addition to excessive theta AP, had excessive delta AP and reduced beta relative power. The difference may also be due to the health differences between Prichep's participants and our participants; as opposed to Prichep et al., we included only participants who had normal levels of cholesterol, glucose, triglycerides, hemoglobin, and thyroid-stimulating hormone, since those physiological parameters are known to impact brain function [41-44].

Excessive theta AP has been reported to predict cognitive decline 7 to 10 years later. The subjects in the present study may be at a preclinical phase in which cognitive difficulties can be compensated for, even though brain function is already compromised, especially because the included subjects were 55 years of age and older and that the sociodemographic characteristics of the sample presented a bias toward higher education. Given that educational level is considered a

proxy of cognitive reserve [47], the negative results obtained could be due to a protective or compensatory effect on cognitive capacity even when neurophysiological alterations have already occurred. These results highlight the advantage of assessing the risk of cognitive decline in older adults using EEG, as it is more sensitive to early changes in brain function than are cognitive–behavioral assessments, regardless of cognitive compensatory mechanisms.

As Rentz et al. [19] established, our findings support the argument that transversal neuropsychological assessments lack sufficient sensitivity to detect subtle cognitive alterations in the preclinical phase of a neurocognitive disorder. It is therefore advised to prioritize the study of neurophysiological markers of risk for cognitive decline with cost-effective instruments such as EEG, including at rest and during task performance (ERPs), which could detect alterations even earlier than neuropsychological tests can.

One of the limitations of this study is the lack of use of established biomarkers in CSF, PET, or genotyping, which could confirm that the sample subjects indeed have a predisposition toward neurodegenerative diseases that result in memory impairments, which could have strengthened our results. Further limitations are a sample bias towards higher education and the fact that we did not assess memory deficits using all available cognitive tests for neuropsychological testing. Future studies should expand on our results by using other neuropsychological tests and methodologies (i.e., longitudinal testing) to corroborate our findings.

In conclusion, the urgency of early detection of pathologic cognitive decline cannot be overstated. Early diagnosis of a neurodegenerative disease and subsequent early treatment can significantly improve the quality of life of patients. Our results suggest that neurophysiological techniques can detect subtle changes in brain function sooner than neuropsychological assessments can, even when high-demand cognitive tests such as the VSTMBT and the LASSI-II are administered,

underscoring the significance of our research. Therefore, it may be desirable to include electroencephalographic recordings in routine neurological assessments of older adults to identify those who are at risk for cognitive impairment. Future investigations should study the relationship between EEG alterations and cognitive decline in longitudinal follow-ups, reinforcing the importance of early interventions and treatments.

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Supporting information

S1 Table. Risk vs. control group differences on the WAIS-IV.

S2 Table. High risk vs. Low risk vs. Control group differences on the median of the sum of zAP(theta).

S3 Table. High risk vs. Low risk vs. Control group differences on the zAP(theta) average.

S4 Table. High risk vs. Low risk vs. Control group differences on the sum of electrodes with excess zAP(theta).

S5 Table. High risk vs. Low risk vs. Control group differences on the sum of zAP(theta) squared (maintaining the sign).