Clinical Neurophysiology 130 (2019) 2222–2230

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Poor working memory performance in healthy elderly adults with electroencephalographic risk of cognitive decline affects syntactic processing

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ARTICLE INFO

Article history:
Accepted 15 September 2019
Available online 15 October 2019

Keywords:
Elderly
Working memory
Syntactic processing
Electroencephalogram
Cognitive decline

HIGHLIGHTS

- Abnormally high values of theta absolute power in older adults hamper sentence processing.
- Older adults at risk of cognitive decline display brain electrical signs of syntactic difficulties.
- EEG risk (excess theta) in older adults might be an indicator for cognitive decline.

ABSTRACT

Objective: To examine the effects of working memory (WM) load and gender agreement on sentence processing as a function of the electroencephalographic risk (i.e., abnormally high values of theta absolute power) of cognitive decline in older adults.
Methods: Event-related potentials (ERPs) were collected from Spanish speakers (22 older adults belonged to the Risk group, mean age = 67.7 years; 22 older adults belonged to the Control group, mean age = 65.2 years) while reading sentences to detect grammatical errors. Sentences varied with regard to (1) the gender agreement of the noun and adjective, where gender of the adjective either agreed or disagreed with the noun, and (2) WM load (i.e., the number of words between the noun and adjective in the sentence).
Results: The Risk group showed a lower percentage of correct answers and longer reaction times than the Control group. The Risk group also showed a different pattern of ERP components, which was characterized by smaller amplitude and longer latency of the P600a component under high WM load conditions.
Conclusion: The findings suggest that the Risk group shows difficulties integrating information associated with the previous sentence context.
Significance: The electroencephalographic risk factor of cognitive decline might be not only a predictor of but also an indicator of current decline.

1. Introduction

Behavioral studies have suggested that verbal performance (reading skills, a wide vocabulary or general intelligence) is preserved in aging (Ronnlund et al., 2005). However, it has been reported that language seems to decline with age (Glisky et al., 2001; McVay and Kane, 2012). Aging also entails other cognitive changes, especially a decline in working memory (WM) and in processing speed (Borella et al., 2008; Park et al., 2002; Rhodes and Katz, 2017).

Electroencephalography (EEG) and cognitive processes are closely related (Niedermeyer and Lopes da Silva, 2005). EEG records the brain electrical activity generated mainly in the neocortex, and the processing of information depends strongly on the functioning of this brain structure (Schomer and Lopes da Silva, 2011).

Resting-state EEG studies have shown that older adults display a brain electrical activity pattern characterized by a diffuse increase in theta absolute power (AP) (Gil-Nagel et al., 2002; Niedermeyer and Lopes da Silva, 2005) and delta AP (Gil-Nagel et al., 2002), as well as a decrease in the frequency and amplitude

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https://doi.org/10.1016/j.clinph.2019.09.009
1388-2457/

of the occipital alpha rhythm (Knyazeva et al., 2018) that topographically reorganizes and spreads to frontal regions (Knyazeva et al., 2018). However, although these EEG features could be associated with normal aging, it has been claimed that these features might reflect some degree of degenerative or cerebral vascular pathology (Chang et al., 2011).

It has been reported that an excess in EEG theta activity (4–7 Hz) in healthy older adults without clinical signs of cognitive decline (e.g., normal Global Deterioration Scale (GDS) scores; Reisberg et al., 1982) constitutes the main electroencephalographic predictor of cognitive impairment in old age (Prichep et al., 2006).

It is known that EEG can be used to measure neuronal dynamics; therefore, it can be used to infer a subject's performance during a cognitive task. The information gained can then be used to determine the subject's clinical condition (Schomer and Lopes da Silva, 2011). However, the studies described above have improved upon this process by demonstrating that the neuronal dynamics recorded by EEG at rest can allow us to make inferences about the future clinical condition of the subject.

Prichep et al.'s study suggested that the elderly population that seems normal is in fact heterogeneous; that is, healthy elderly people could be split into at least two groups. Both groups have no clinical signs of cognitive impairment, but the group with abnormally high theta AP values may be at risk for future cognitive decline. A study described these EEG patterns as indicative of a shadow zone between normality and the preclinical stages of dementia (Babiloni et al., 2006). In accordance with the above, we have shown that there are two cognitive subgroups within healthy older adults (Sánchez-Moguel et al., 2018). Using ERPs during a counting Stroop task, we explored inhibitory control processes in healthy elderly participants with an EEG risk of cognitive decline (i.e., an excess of theta activity in their EEG) versus a group of healthy elderly participants with normal EEG. The results suggested that the group at risk displayed a failure in the automatic reading process. In this respect, it has been proposed that inefficient inhibitory control can allow easy access of irrelevant information to WM systems that could subsequently affect language processing (Hasher and Zacks, 1988). However, this mechanism is not sufficient to explain all age-related changes in language processing.

Aging effects on language processes are still debated today. It has been suggested that aging affects a major component of the language system, and it has been proposed that the component that fails is the WM system (Cohen, 1988). Behavioral studies of aging have supported Cohen's proposal because elderly subjects seem to manifest more difficulties in language comprehension when the syntactic structure of the sentence is more complex (Kemper, 1987; Kemper et al., 2001). That is, more complex sentences require greater resources from the WM system because grammatical information of all lexical units is maintained in the WM system. However, the resources of the WM system seem to result in a decreased capacity for grammatical information (Just and Carpenter, 1992).

ERP studies in young adults have demonstrated a failure to maintain linguistic features in WM during syntactic processing when WM load was increased. WM load can be manipulated by length or syntactic complexity (i.e., the number of words in a sentence or number of nodes parsed, respectively). For instance, greater length or syntactic complexity has been associated with decreased processing speed and difficulties in sentence comprehension (King and Just, 1991; Vos et al., 2001; McVay and Kane, 2012). Young adults have displayed a greater cost of neural processing reflected in the modulation of ERPs when WM load was higher. The LAN (left-anterior negativity: 300–500 ms) component is modulated by morphosyntactic violation detection (Bornkessel and Schlesewsky, 2006; Molinaro et al., 2011). Therefore, a greater LAN amplitude is expected when a morphosyntactic error appears. Vos et al. (2001) described greater LAN amplitude differences between grammatical agreement conditions when the WM load had been increased.

Another ERP effect of increased WM load is the modulation of the P600 component (i.e., positivity between 500 to 900 ms), which presented smaller amplitudes (Gunter et al., 1997; Kolk et al., 2003; Alemán-Bañón et al., 2012) and longer latencies with increases in sentence length (Phillips et al., 2005; Vos et al., 2001). It is well known that the P600 component is also modulated by syntactic reanalysis processing (Molinaro et al., 2011), and this component can be divided into two processing stages: P600a and P600b (Barber and Carreiras, 2005; Silva-Pereyra and Carreiras, 2007). The first has been associated with the integration of the previous sentence context with the critical word (Barber and Carreiras, 2005; Kaan et al., 2000; Silva-Pereyra and Carreiras, 2007), and the second has been linked to the repairing of anomalous features of the sentence (Barber and Carreiras, 2005; Kolk et al., 2003; Molinaro et al., 2011; Silva-Pereyra and Carreiras, 2007).

There could be a direct effect of aging on language associated with age-related changes in the WM system. Normal aging has been associated with preserved verbal performance when greater demands on the WM system are not required (i.e., reading skills and vocabulary size) (Ronnlund et al., 2005). However, ERP studies have also described age-related changes in the neural pattern of language processing compared with young adults (Wlotko et al., 2010). Specifically, although behavioral performance remains preserved, older adults displayed a more widespread distribution of the P600 agreement effect (Kemmer et al., 2004). Concerning the effects of age-related changes in WM and language processing, there are no studies that address such effects in this population; however, older adults show a systematic decline in this WM system (Borella et al., 2008; Park et al., 2002), which is more severe when subjects show cognitive impairment; hence, the effects of increased WM load on language could be different between groups with or without electroencephalographic risk of cognitive decline.

Considering that (a) older adults are distributed into two populations with different electroencephalographic features (i.e., normal EEG and excess of theta activity) but a preserved behavioral performance and (b) high WM load seems to affect language comprehension in the context of poor behavioral performance and an electrophysiological pattern that reflects higher costs of neural processing, we decided to explore the effect of WM load (i.e., syntactic complexity) and gender agreement on sentence processing as a function of the electroencephalographic risk of cognitive decline. We hypothesized that older adults with a risk of cognitive decline will show poorer behavioral performance (i.e., fewer correct answers and longer response times with high WM load) and greater cost of neural processing than the group with normal EEG when WM load is increased, supported by the amplitude or the latency of the ERP components; in particular, older adults with risk of cognitive decline would show greater amplitude of LAN as a reflection of morphosyntactic problems and smaller amplitude and longer latency of the P600 effect as evidence of additional difficulty in integrating information of the previous sentence context and a generalized mapping of the sentences.

2. Materials and Methods

2.1. Participants

Fifty right-handed Mexican adults over the age of 60 were recruited. Right-handedness was assessed with a brief Spanish version of the Edinburgh Handedness Inventory (LQ > +50; Oldfield, 1971). They were native Spanish speakers and healthy. Participants did not present signs of hypercholesterolemia, anemia, diabetes, thyroid disease or uncontrolled hypertensive disease in clinical blood analysis. All subjects were assessed by a specialist in the area of geriatric psychiatry to exclude participants based on any psychiatric or neurological disorder. Psychiatric examination included GDS (Reisberg et al., 1982); all participants obtained scores of 1 or 2 in this scale, indicating that our sample did not show behavioral evidence of cognitive decline. They had at least 9 years of schooling and scored more than 90 on the Spanish version of the Wechsler Adult Intelligence Scale (WAIS, Wechsler, 2003). This scale had four index scores: verbal comprehension (VC), working memory (WM), perceptual organization (PO), and processing speed (PS). All subjects were informed of their rights and provided written informed consent for participation in the study. This study was approved by the Ethics Committee of the Instituto de Neurobiología at the Universidad Nacional Autónoma de México (Ref: INEU/SA/CB/109).

Eyes-closed resting EEG was recorded for 15 minutes with a Medicid IV system (Neuronic Mexicana, S.A., Mexico) and Track Walker TM v5.0 data system from 19 leads of the 10–20 system (ElectroCap, International Inc.; Eaton, Ohio, USA) using linked earlobes (A1A2) as a reference. The signal was amplified with a gain of 20,000, and the bandwidth was set between 0.5 and 50 Hz. Impedances were kept below 5 kΩ, and the sampling rate was 200 Hz (5 ms). Twenty-four artifact-free segments of 2.56 seconds were used for quantitative analysis that was performed offline. The data were fast Fourier transformed to obtain cross-spectral matrices every 0.39 Hz, and the geometric power correction was applied to the (AP) measure (Hernández et al., 1994); this correction makes a rescaling of the power spectrum, leading to the removal of around 42% of the variability not related to physiological factors. Z scores were calculated for AP and relative power (RP) in four frequency bands: delta (1.5–3.5 Hz), theta (4–7.5 Hz), alpha (8–12.5 Hz) and beta (13–19.5 Hz). Subject's measures were compared with a normative database (Valdés et al., 1990), and Z-values <1.96 were considered in all bands and electrodes within normal limits for the subject's age. Additionally, visual inspection of the EEGs was performed by an expert electroencephalographer.

Six participants who presented abnormalities other than theta excess were invited to participate in other projects. As Fig. 1 shows, the remaining 44 participants were classified into two groups: the Risk and the Control groups. The Risk group was formed by subjects with theta AP Z-values higher than 1.96 in at least one lead, and the Control group was composed of subjects with AP and RP Z-values lower than 1.96 in all leads and all bands, and they did not present abnormal waves.

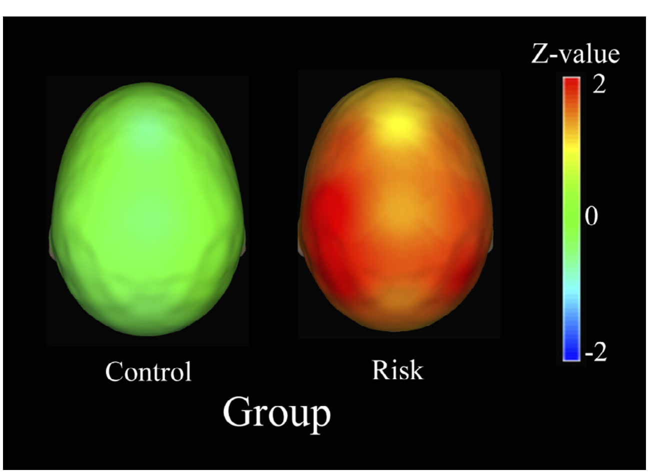

Fig. 1. Statistical Z maps of theta AP. The AP of the Risk group is higher than that of the Control group, reaching abnormal values in some regions, mainly in the left hemisphere.

The Risk group consisted of 22 subjects (mean age = 67.7 years old, standard deviation (SD) = 5.8; range = 60–81 years old; female/male = 12/10), and the Control group was formed by 22 older adults (mean age = 65.3 years old, SD = 3.8; range = 60–74 years old; female/male = 15/7). Table 1 shows the sample demographic information and their scores on the WAIS test. Both groups were matched in age, scholarship (years), and sex. The Risk and the Control groups were compared by the subscales of each WAIS index. Four mixed two-way ANOVAs were performed with Group (Risk and Control) as a between-subjects factor, and a) vocabulary, similarities, and information (VC index), b) arithmetic, digit span, and letter-number sequencing (WM index), c) block design and matrix reasoning (PO index) and d) digit symbol coding and symbol search (PS index) were included as within-subjects factors for each ANOVA. No significant differences between groups were observed for the VC and WM indices. However, for the PO index, the Control group (block design: mean = 12.2, SD = 3.1; matrix reasoning: mean = 11.3, SD = 3.0) performed better than the Risk group (block design: mean = 9.8, SD = 2.4; matrix reasoning: mean = 9.9, SD = 22.6). Similarly, for the PS, the Control group (digit symbol coding: mean = 12.0, SD = 2.6; symbol search: mean = 11.8, SD = 2.0) performed better than the Risk group (digit symbol coding: mean = 10.1, SD = 2.7; symbol search: mean = 10.3, SD = 2.0).

2.2. Stimuli and procedure

Two hundred and twenty Spanish sentences composed of seven words were built from a Mexican computerized word-frequency use database of Spanish (LEXMEX; Silva-Pereyra et al. 2014). We selected nouns, verbs and adjectives based on their frequency of use (words were included with above 30 appearances/million). The sentences varied according to "gender agreement" (agree or disagree). To build the disagreement sentences, the gender morpheme of the adjective was changed, i.e., the feminine amarill**a** to the masculine amarill**o** (feminine yellow to masculine yellow); in Spanish, the last morpheme indicates the gender. All nouns denominated inanimate objects, and the gender proportion was the same for agree and disagree sentences. WM was manipulated with two levels of load (low and high). To build the high WM load condition, a clause was inserted between the noun and adjective. Meanwhile, in the low WM load condition, no word was inserted between lexical units. Eighty sentences were agreement sentences, and eighty were disagreement sentences. Forty agreement sentences had low WM loads, and the remaining 40 had high WM loads. The same distribution was used for disagreement sentences. Sixty filler sentences were also included, consisting of 30 ungrammatical and 30 grammatical (with or without a number agreement violation between the noun and adjective). Table 2 displays some stimulus examples.

The stimuli were delivered to subjects with STIM2 software (Neuroscan, Compumedics, North Carolina, USA) on a computer screen while they were seated 70 cm away from the screen in a dimly lit faradized and soundproof room. The task instructions were presented on the screen. Participants had to read the whole sentence and respond as quickly and accurately as possible only when the question marks appeared. All words and symbols (Arial, 80 points) were in white with a black background. First, a cross was presented at the center of the screen for 300 ms as a fixation point; later, each word appeared for 300 ms with an interstimulus interval of 300 ms. The whole sentence was presented word by word, and at the end, the question marks appeared for 1500 ms. Participants judged the grammaticality of the sentences by

Table 1
Demographic and cognitive variables in older adults: Control and Risk groups.*

	Group	Mean (SD)	T(42)	p-value
Age (years)	Control group	65.3 (3.8)	1.66	0.10
	Risk group	67.7 (5.8)		
Scholarship (years)	Control group	16.7 (5.6)	−1.14	0.26
	Risk group	15.1 (3.9)		
	Group	Percentage	χ^2 (1)	p-value
Sex	Control group	68.2% (F)	0.35	0.54
	Risk group	54.5% (F)		
ANOVAs Group (Risk and Control) by WAIS indices				
Indices	Effects	F (1, 42)	p-value	η^2p
VC	Group	<1		
	Group by VC interaction	<1		
WM	Group	<1		
	Group by WM interaction	1.0#	0.371	0.02
PO	Group	6.4	0.010	0.13
	Group by PO interaction	<1		
PS	Group	7.5	0.009	0.15
	Group by PS interaction	<1		

* SD, standard deviation; F, female; VC, verbal comprehension; WM, working memory; PO, perceptual organization; PS, processing speed, # F(2,84) Greenhouse-Geisser epsilon = 0.989.

Table 2
Examples of stimuli presented to the subjects.*

WM Load	Agreement	Example
Low	A	La <u>casa</u> **amarilla** está en la colina[1]
	D	El <u>carro</u> **amarilla** está en la colina[2]
High	A	La <u>casa</u> que está allá es **amarilla**[3]
	D	El <u>carro</u> que está allá es **amarilla**[4]

* a, agree; d, disagree. Nouns are underlined and adjectives are typed in bold fonts.
[1] The **yellow** <u>house</u> is on the hill.
[2] The **yellow** <u>car</u> is on the hill.
[3] The <u>house</u> over there is **yellow**.
[4] The <u>car</u> over there is **yellow**.

pressing a button on a response box. One button was for "correct" agreement sentences, and the other button was for "incorrect" disagreement sentences. Among subjects, response buttons were counterbalanced. The participants had three periods to rest: once every 9 minutes. The task lasts 35 minutes.

2.3. ERP acquisition

The EEG was recorded using 32 Ag/AgCl electrodes embedded in an elastic cap (Electro-cap, International, Inc.) and was amplified using a bandwidth of 0.1–100 Hz (Neuroscan SynAmps system, Compumedics, NC, USA) with a sampling rate of 500 Hz. Electrode impedances were kept below 2 kΩ. EEG recordings were referenced online to left earlobe (A1) and right earlobe was record (A2). EEG was re-referenced offline to the average of the earlobe electrodes (A1-A2). Blinks and eye movements were monitored by two electrodes located on the external supraorbital ridge and canthus of the left eye. The eye-movement correction algorithm from Scan 4.5 software tools (Neuroscan, Compumedics) was applied to remove ocular-movement artifacts. Low-pass filtering for 50 Hz and a 6-dB slope was performed offline.

Automatic rejection of segments was performed based on two criteria: Segments with amplifier blocking for more than 50 ms and EEG epochs (−200 to 1000 ms) with voltage amplitude exceeding ± 50 μV at any electrode site were considered artifact, and the entire segment was rejected. In the remaining epochs a baseline correction was performed using the 200-ms pre-stimulus time. Only artifact-free trials were included in the averages. No significant differences between experimental conditions with respect to the number of artifact-free segments were observed (F < 1, approximately 95% of the data for each of the conditions).

2.4. Data analysis

2.4.1. Behavioral data

The statistical analysis of the percentage of correct answers and the response times (RTs) were separately carried out through two mixed three-way ANOVAs. Group (Control and Risk) was included as the between-subjects factor, and gender agreement (agree and disagree) and WM load (high and low) were included as within-subjects factors. To ensure a normal distribution of the data, percentages of correct answers were transformed using the function ARCSINE [square root (percentage/100)]. Tukey's Honest Significant Difference (HSD) method was used for *post hoc* pairwise comparisons.

2.4.2. ERP data

ERPs were obtained offline using epochs of 200 ms prestimulus and 1000 ms poststimulus linked to the adjective in each sentence. EEG segments of each experimental condition (i.e., agree/disagree and high/low WM load) were averaged for each participant. Averaged waveforms included only correctly answered trials with voltage changes lower than ±50 μV. Baseline correction was performed using the 200-ms prestimulus time window. There were ERP waveforms associated with gender agreement processing that have been previously described in the literature (Bornkessel and Schlesewsky, 2006). A negative wave over the left anterior region between 300 and 500 ms (i.e., LAN) followed by a positive waveform between 500 and 900 ms (i.e., P600) were observed.

2.4.2.1. Amplitude analyses of ERPs. Mean amplitude data from 300 to 500 ms was considered for the statistical analysis of LAN. The positive wave occurring between 500 and 900 ms was divided into two windows for analysis as others have done (Barber and Carreiras, 2005; Kolk et al., 2003; Vos et al., 2001; Silva-Pereyra and Carreiras, 2007): 500–700 ms (P600a) and 700–900 ms (P600b). For the P600a and P600b the mean amplitude was also calculated. Difference waves (i.e., ERPs of the disagree condition minus ERPs of the agree condition) were also calculated, and latency values (i.e., the maximum amplitude within the range of the component's window) were determined from the ERPs.

Statistical analysis of the amplitude and latency of ERP waveforms and difference waves were performed in each time window (i.e., LAN, P600a and P600b) using a nonparametric permutation method. The analyses were performed using the statistical module included in the standardized low-resolution brain electromagnetic tomography software (Pascual-Marquí, 2018; http://www.uzh.ch/keyinst/loreta.htm). This method is based on estimation of the empirical probability distribution for the maximum t statistic under the null hypotheses. The distribution is created from the data via randomization by iteratively shuffling the condition labels over trials (for within-subject analyses) or over subjects (for group-level analyses) and recomputing the test statistic. This method corrects for multiple testing. All electrode locations (i.e., FP1, FP2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, T6, Cz, Fz, Pz, FCz, CPz, CP3, CP4, FC3, FC4, TP7, TP8, FPz, Oz, FT7, FT8) were considered in the comparisons.

The amplitude of ERP waveforms was analyzed as follows: (a) we compared agreement condition differences between groups (i.e., Control and Risk group) of each ERP component for each WM load factor (i.e., high or low WM load conditions; Ho: A1-A2 = B1-B2). Comparisons within groups were also calculated between agreement conditions (i.e., agree and disagree) to explore LAN, P600a and P600b effects in each group. Additionally, Pearson's correlations between LAN or P600a effects and AP Z-values of theta band in high WM load conditions were performed. (b) We also explored the gender agreement effect of each component (i.e., greater amplitude for the disagree than agree condition) regardless of WM load condition (i.e., group by agreement interaction). Analyses were performed using five thousand permutations. P-values resulting from a set of comparisons were corrected by the false discovery rate (FDR) method. Benjamini-Hochberg adjusted P-values are reported, and corrected P-values <0.05 were considered statistically significant (https://tools.carbocation.com/FDR).

2.4.2.2. Latency analyses of ERPs. Two mixed three-way ANOVAs using latency data were separately performed within the range of the P600a and P600b windows. Three electrode locations (FCz, Cz and, CPz) and WM load conditions were included as within-subjects factors, and the group was considered a between-subjects factor for the P600a window. Midline electrode locations (Cz, CPz and Pz) and WM load were considered within-subjects factors, and group was considered a between-subjects factor for the P600b window. Electrode locations analyzed for the latency analyses were selected from previous literature examining the topography of these components (Molinaro et al., 2011).

3. Results

3.1. Behavioral results

As shown in Fig. 2, differences between groups were observed in the percentage of correct answers [Group: $F(1,42) = 4.65$, $p = 0.04$, $\eta^2p = 0.10$]. The Control group had a higher percentage of correct answers than the Risk group. Regarding reaction times, the Risk group was significantly slower than the Control group [Group: $F(1,42) = 4.62$, $p = 0.04$, $\eta^2p = 0.10$] in all experimental conditions. No significant interactions of any experimental condition by group were observed in the accuracy of responses or reaction time analyses.

3.2. Electrophysiological results

3.2.1. Amplitude analyses

3.2.1.1. WM load.

3.2.1.1.1. Low WM load condition. *LAN:* As shown in Fig. 3, differences between groups were observed ($t_{max} = 1.84$, $p = 0.03$). The Control group displayed a greater LAN effect than the Risk group in the FP1, FP2, FPz, F4, FT7, FT8 TP7, TP8 and Oz electrodes. Comparisons within groups between agreement conditions showed that both groups did not display a significant LAN effect in this WM load condition (Control group: $t_{max} = 1.85$, $p = 0.30$; Risk group: $t_{max} = -1.87$, $p = 0.06$).

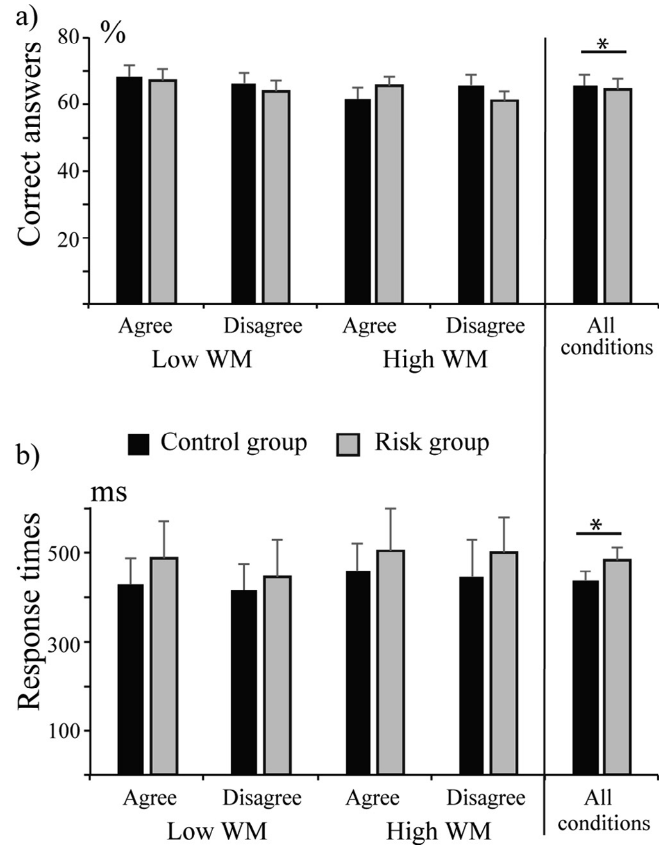

Fig. 2. Behavioral results: a) Percentage of correct answers for both groups at the two WM load conditions; b) Response times across all conditions (extreme right) showed significant differences between groups.

P600a: No differences between groups in the P600a effect were observed ($t_{max} = 1.79$, $p = 0.06$); in addition, comparisons within groups between agreement conditions showed that both groups did not display significant P600a effects when the WM load was low (Control group: $t_{max} = 1.87$, $p = 0.23$; Risk group: $t_{max} = 2.66$, $p = 0.90$).

P600b: No differences between groups in the P600b effect were observed in this WM load condition ($t_{max} = 1.83$, $p = 0.23$). Comparisons within groups between agreement conditions showed that both groups displayed a significant P600b effect in this WM load condition (Control group: $t_{max} = 1.89$, $p = 0.003$; Risk group: $t_{max} = 1.80$, $p = 0.009$). The Control group displayed P600b effects in the F3, C3, P3, O1, T6, Fz, and CP3 locations, while the Risk group showed P600b effects at the following sites: C4, P4, O2, T4, and T6.

3.2.1.1.2. High WM load conditions. *LAN*: No differences between groups were observed in the LAN effect when the WM load was high ($t_{max} = 1.93$, $p = 0.70$). Comparisons within groups between agreement conditions showed significant LAN effects. The Control group displayed this effect at the following sites: FP2, Cz, Pz, FCz, CPz, CP4, FC4, TP7, TP8, FPz, Oz, FT7, and FT8 ($t_{max} = 1.89$, $p = 0.03$). The Risk group showed the LAN effect at electrodes F4, C4, T3, FCz, CP4, FC4 and TP8 ($t_{max} = 1.99$, $p = 0.01$). Additionally, as shown in table 3, there were negative correlations between the LAN effect at F7 and T3 and AP Z-values of the theta band; that is, greater AP Z-values of the theta band were correlated with a smaller LAN effect.

P600a: As shown in Fig. 3, differences between groups were found in the P600a effect ($t_{max} = 1.85$, $p = 0.05$). The Control group displayed a greater P600a effect than that observed in the Risk

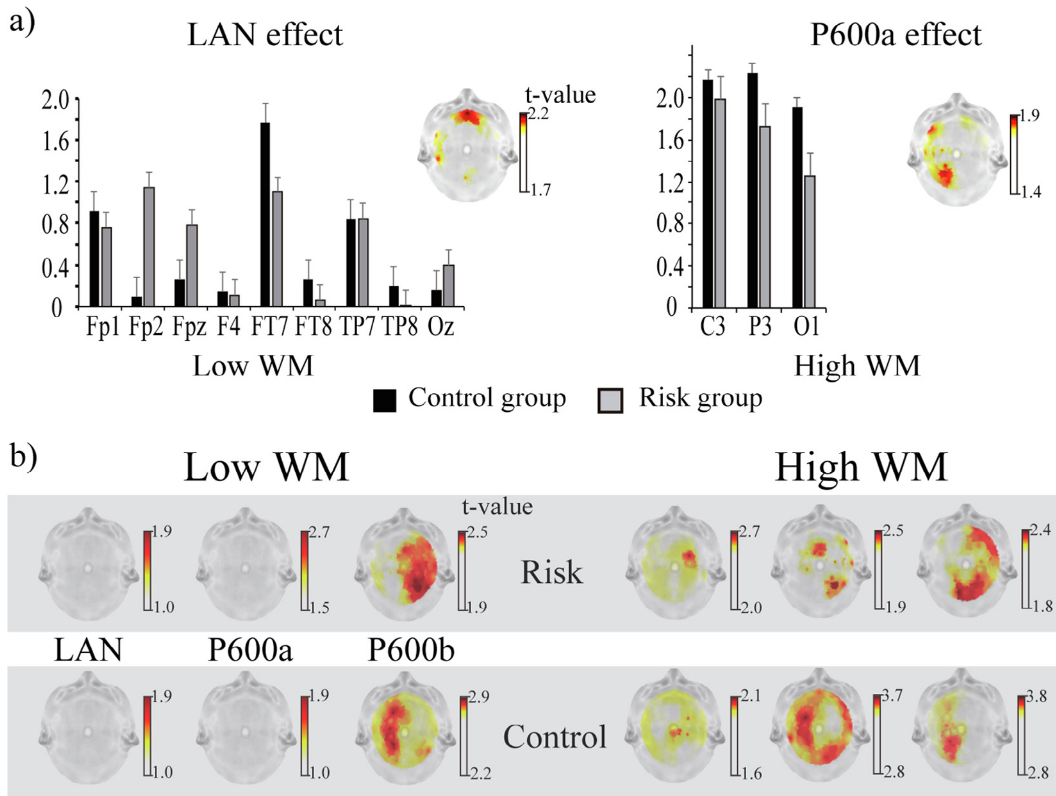

Fig. 3. Statistical nonparametric comparisons between groups and conditions: a) Significant amplitude differences between groups in the LAN (left) and P600a (right) effects in low and high WM load conditions, respectively; b) Significant amplitude differences between agreement conditions (disagree minus agree) for each group. The colored scale indicates significant t-values (p < 0.01 in red and p < 0.05 in yellow). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 3
Significant Pearson's correlations between AP Z-values of theta band and LAN effect in the high WM load condition.

Electrodes	Theta AP Z-values		LAN effect	
	Mean (SD)		F7	T3
	Risk	Control	r values (n = 44)	
FP2	1.12 (0.87)	−0.01 (0.86)	−0.39**	−0.40**
F3	1.02 (0.95)	−0.13 (0.92)		−0.34*
F4	1.71 (1.24)	−0.08 (1.03)	−0.37*	−0.45**
C3	1.58 (1.31)	−0.11 (1.02)		−0.37*
C4	2.14 (1.27)	−0.19 (1.07)	−0.48**	−0.51**
P3	1.76 (1.42)	−0.07 (1.06)	−0.40*	−0.41**
P4	2.12 (1.60)	−0.28 (0.92)	−0.50**	−0.36*
O1	2.00 (1.57)	−0.00 (0.93)	−0.43**	−0.36*
O2	1.41 (1.15)	−0.37 (0.82)	−0.45**	−0.45**
F7	1.22 (1.08)	−0.39 (0.95)	−0.37*	
F8	1.50 (0.85)	0.21 (0.69)	−0.31*	−0.44**
T4	1.27 (0.85)	−0.33 (0.76)	−0.49**	−0.48**
T6	1.66 (1.11)	−0.31 (0.77)	−0.55**	−0.49**
FZ	1.17 (0.95)	−0.08 (0.54)	−0.42**	
CZ	0.99 (1.15)	−0.57 (0.89)	−0.33*	−0.42**
PZ	1.43 (1.05)	−0.39 (1.00)	−0.39**	−0.45**

p-values: * p < 0.05, ** p < 0.01.

Group at the C3, P3, O1, and F7 sites. Comparisons within groups showed a significant P600a effect for both groups (Control group: t_{max} = 1.86, p = 0.0006; Risk group: t_{max} = 1.90, p = 0.01). The Control group showed the P600a effect mainly at the P3, O2, F8, T6, CP3, FC3, TP7, and FPz sites, and the Risk group displayed this effect in the following locations: C4, P4, F8, T4, T6 and FCz. No significant correlations were found between the P600a effect and the AP Z-values of the theta band.

P600b: No differences between groups were observed in the P600b effect (t_{max} = 1.85, p = 0.20). Comparisons within groups showed a significant P600b effect (Control group: t_{max} = 1.83, p = 0.001; Risk group: t_{max} = 1.84, p = 0.02). The Control group mainly showed the P600a effect at the F3, C3, P3, O1, Cz, and Pz sites, and the Risk group displayed this effect in the following locations: FP2, F4, C4, P4, O1, O2, F8, Oz, and FT8.

3.2.1.2. The gender agreement effect. LAN: The Control group displayed a greater LAN effect (i.e., greater amplitude for disagree than the agree condition) than the Risk group (t_{max} = 1.87, p = 0.03) at the following electrodes: FP1, FP2, F3, F4, F8, T4, T5, Cz, Pz, CPz, FC3, TP7, TP8, FPz, Oz, FT7 and FT8. *P600a:* The Control group showed a greater amplitude of the P600a effect than the Risk group regardless of WM load condition (t_{max} = 1.83, p = 0.02) at the following sites: FP2, F4, F7, T3, T4, and Cz. *P600b:* No differences between agreement conditions were observed between groups regardless of WM load condition (t_{max} = 2.14, p = 0.22).

3.2.2. Latency analyses

P600a: Fig. 4 shows differences in latency between groups; a significant interaction for group by WM load condition by gender agreement by electrode was found [F(2,84) = 7.66, p = 0.002, η^2p = 0.15, ε = 0.79]. A post hoc test showed that the Risk group displayed longer P600a latencies in the high WM load condition than the Control group in the CPz location (MD = 57.18, p = 0.01). In addition, the Control group displayed a longer P600a latency for high than low WM load conditions (Cz: MD = -57.45 ms, p = 0.02; CPz: MD = 67.64, p = 0.005). Meanwhile, the Risk group did not display these differences (Cz: MD = 21.72 ms, p = 0.36; CPz: MD = 3.36, p = 0.88). No main effect of Group was observed (Group: F < 1).

P600b: No differences in P600b latency between groups were observed (Group: F < 1). No significant interactions of WM load or gender agreement by group were observed at this latency.

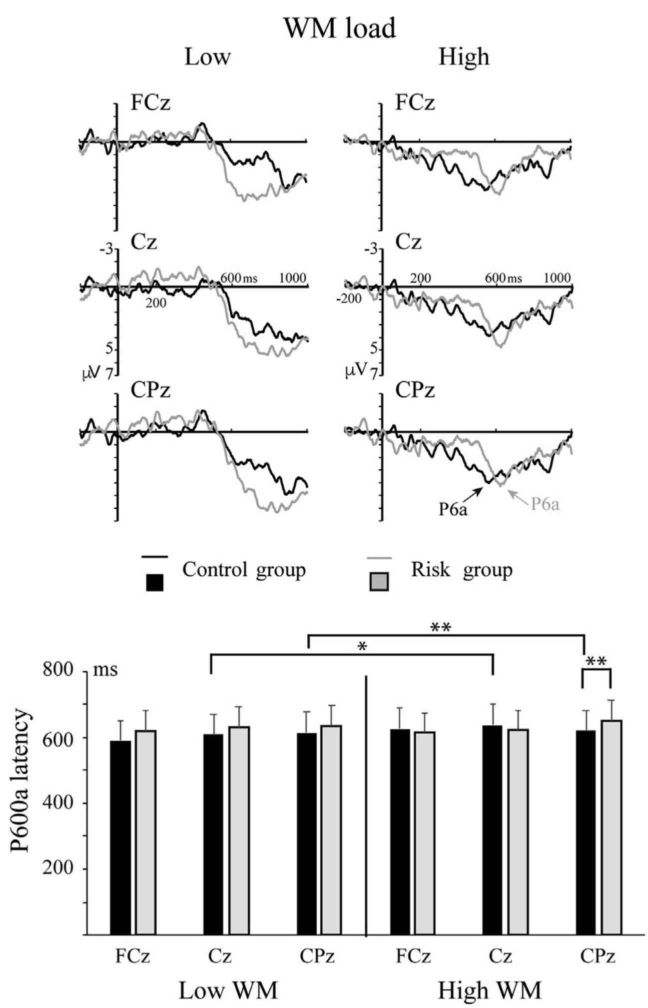

Fig. 4. Latency differences between groups: a) ERP difference waves (i.e., disagree condition minus agree condition) from both the Risk and Control groups by WM load at three midline electrodes (FCz, Cz and CPz). Negative is plotted up. Arrows indicate the maximum positive peaks of the P600a component, and asterisks indicate significant differences (*p < 0.05; **p < 0.01).

4. Discussion

This study aimed to identify behavioral and electrophysiological differences in the effects of WM load on gender agreement processing between two groups of older adults: one group with an electroencephalographic risk of cognitive decline and another group with a normal EEG.

4.1. Behavioral evidence

Considering that in aging, sentence processing may be affected by increases in WM load and that the Risk group may have shown a greater decline in WM than the Control group, we predicted that with high WM load, older adults with excess theta in their EEG would show greater processing cost than older adults with normal EEG reflected in a poorer behavioral performance (i.e., a lower percentage of correct answers and longer reaction times). The results partially agreed with our hypothesis; differences between groups in the accuracy of responses and reaction times were observed regardless of WM load. The Risk group had a lower percentage of correct answers and longer reaction times than those observed in the Control group. These results may indicate that the cognitive changes related to the EEG risk factor involve not only changes in WM but also changes in sentence processing, which was reflected by a greater difficulty in detecting the morphosyntactic violations in low WM load conditions in the Risk group.

Syntactic processing seems to manifest few age-related changes and has been considered a part of crystallized intelligence (Stine-Morrow et al., 2008). Refuting this postulate, Zhu et al. (2018) observed that older adults displayed poorer behavioral performance than young adults when performing a syntactic agreement task; however, Alatorre-Cruz et al. (2018) described that older adults may have similar behavioral performance to young adults in syntactic processing, supporting the hypothesis of syntactic processing as a part of crystallized intelligence. An essential difference between these two studies lies in the fact that the former did not require a normal EEG of the subjects as an inclusion criterion, while the latter did. This suggests that the normality of the EEG could be important to have an appropriate behavioral performance in syntactic processing in aging (Alatorre-Cruz et al., 2018).

However, the electroencephalographic risk factor of cognitive decline may have interfered in sentence processing due to changes in other cognitive processes, such as decreases in processing speed or changes in executive control mechanisms. Evidence for lower processing speed in the Risk group than in the Control group may be supported by results on the WAIS-III (the processing speed index was lower in the Risk group than the Control group) and in the reaction times observed in our task of morphosyntactic agreement (longer reaction times for the Risk group than the Control group). Accordingly, decreased processing speed may have disrupted response accuracy due to subprocesses of sentence processing that might not have been completed when the subject had to provide a response. In this respect, aging studies have shown that older adults display lower processing speed than young adults when they make a response (Cerella and Hale, 1994); this fact has been considered a characteristic of aging. In this study, both groups had similar chronological ages, but the Risk group manifested a processing speed that was more similar to that observed in an older group.

A complementary explanation is that the Risk group may have used a different mechanism of executive control than the Control group. It has been reported that older adults use different mechanisms than young adults to resolve tasks; young adults use proactive mechanisms, while older adults use reactive mechanisms (Braver et al., 2009). The proactive mechanisms rely on anticipation of the event before it occurs, and reactive control relies on the detection and resolution of the event after its onset (Braver et al., 2009). Therefore, reactive mechanisms may have resulted in longer reaction times because the subject did not anticipate the processing needed to generate the response. In this study, the Risk group may have displayed a reactive mechanism due to problems anticipating the event; meanwhile, the Control group used a mechanism more similar to that observed in young adults, resulting in better reaction times. This fact may be explained by the electrophysiological characteristics of the Risk Group; it has been reported that older adults display a brain electrical activity pattern characterized by a diffuse increase in theta AP (Gil-Nagel et al., 2002), and this pattern seems to increase with age. Therefore, the Risk group seems to manifest the electroencephalographic characteristics of an older group. It is well known that declines in the mechanisms of executive control have been associated with aging (Cerella and Hale, 1994); consequently, the deficits in executive control that are apparent in the Risk group should be associated with this EEG risk factor.

4.2. ERP evidence

The electrophysiological evidence partially agreed with our expectations. Although we expected to find differences between groups only in the high WM load condition, differences were observed in both WM load conditions. With a low WM load, the Risk group showed fewer amplitude differences in the LAN component between the agreement conditions than the Control group. Theoretically, LAN has been associated with the retrieval of lemma from the lexicon (i.e., morphosyntactic processing; Bornkessel and Schlesewsky, 2006; Molinaro et al., 2011). Studies examining grammatical agreement have described a greater ERP amplitude in disagree conditions than in agree conditions because the disagree condition requires extra processing due to the grammatical violations. Therefore, the Risk group may have shown greater problems than the Control group in distinguishing the agreement conditions because these conditions required more resources or there was a lower availability of resources to process the disagree sentences. For both possible explanations, the Risk group may have been manifesting problems in morphosyntactic processing, even when the WM load condition was low. The evidence of the problem in morphosyntactic processing may have also been observed in the amplitude of the LAN effect where, regardless of the WM load, the Risk group had a smaller effect than the Control group.

In the high WM load conditions, we expected that the Risk group would show a greater LAN effect, smaller P600 effect, and longer P600b latency than the Control group. Although the expected differences in the high WM load condition between groups were not observed in the LAN effect, we found that the Risk group seemed to manifest a smaller LAN effect as AP Z-values of the theta band increased. Although this finding did not match one of our hypotheses, it may have reflected a problem in morphosyntactic processing because a smaller LAN effect reflects a poorer differentiation between agreement conditions (Alatorre-Cruz et al., 2018).

At the next level of processing, there was a greater P600a effect in the Control group than in the Risk group, which matched our hypothesis. Prior studies have reported a smaller P600 effect as the WM load increased, but these studies compared young participants with older adults (Gunter et al., 1997; Kolk et al., 2003; Phillips et al., 2005; Vos et al., 2001). This finding has been interpreted as a greater use of neural resources. Therefore, our results are supported by this interpretation and suggest that the Risk group required more neural resources to process the sentences; hence, in this study, the Risk group had greater difficulties than the Control group in integrating the information because the P600a component has been linked with the integration of all information associated with the previous sentence context (Barber and Carreiras, 2005; Kaan et al., 2000). Additional evidence of the difficulties in integrating the information of the sentence for the Risk group may be found in the amplitude of the P600a effect regardless of the WM load. The Risk group showed a smaller P600a effect than the Control group. A further difficulty at this level of processing may also be explained by the problem in morphosyntactic processing that occurred in the previous stage.

It was also expected that the Risk group would show longer latency than the Control group in the P600b component as an effect of difficulties in initiating the general mapping of the sentence because this processing requires more from WM. However, differences in latency between groups were found earlier at P600a; this finding may also support the Risk group having more difficulties integrating information from the sentence than the Control group. In addition, the Control group showed a longer latency of the P600a effect with the high than with the low WM load; meanwhile, the Risk group did not show differences between WM load conditions. This finding may be explained as a problem discriminating between WM load conditions for the Risk group.

4.3. Overview

The behavioral performance of gender agreement processing was different between groups; the Risk group showed worse behavioral performance (i.e., longer reaction times and a lower percentage of correct answers) regardless of WM load condition. Hence, it seems that the electroencephalographic risk predictor of cognitive decline may be a part of a mechanism associated with failures in both sentence processing and WM. However, other cognitive processes may be related to this failure. For example, it is probable that participants in the Risk group were using a reactive mechanism; it prevented them from anticipating the event, generating a worse behavioral performance in the task.

Even when the behavioral performance and electrophysiological results were not completely consistent with our hypothesis, the electrophysiological pattern in both groups matches our behavioral findings. The brain response pattern was consistent with the idea of a failure in sentence processing in the Risk group. Older adults with risk seem to have problems at the first level of processing (i.e., morphosyntactic), which is supported by the differences between groups in the low WM load condition (the Risk group showed a smaller amplitude difference of ERPs between the agreement conditions than the Control group) and a smaller LAN effect regardless of WM load. This may have indicated that the Risk group had a problem discriminating between agreement conditions.

Our results also seemed to indicate that when the WM load was high, the Risk group showed greater difficulty integrating information associated with the previous sentence context; this problem was evidenced by the smaller P600a effect in this group, the smaller P600a effect regardless of the WM load, longer P600a latencies and no effect of higher WM load on latency, which is evidence of difficulties maintaining information in WM.

5. Conclusion

We conclude that the electroencephalographic risk of cognitive decline seems to be associated with problems in morphosyntactic processing and problems in WM; this conclusion suggests that the risk factor is not only a predictor but also an indicator of cognitive decline.

Acknowledgements

We thank Susana A. Castro-Chavira, Lourdes Lara, Teresa Álvarez, Sergio M. Sánchez-Moguel, Leonor Casanova and Héctor Belmont for administrative and technical support.

Funding

This research was funded by Universidad Nacional Autónoma de México, México (PAPIIT- DGAPA, projects IN225414 and IN200817) and CONACYT, México (Grant #290915).

Disclosure Statement

The authors have no conflicts of interest to declare.

Author Contributions

GA, JSP, and TF designed the research. GA and TF acquired the data. JSP, GA, TF, and MR analyzed the data. GA, JSP, TF, and MR contributed to data interpretation and to the writing of the paper.

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