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Cognitive reserve correlates with task-related EEG power in healthy aging

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Abstract:
Background*: Cognitive reserve (CR) is a neuroprotective factor that allows persons to mitigate the impact of negative conditions such as dementias. Neurophysiological techniques such as electroencephalography facilitate the observation of the functional dynamics of cognitive processes. Recently, research models have been designed to study cognitive reserve using neurophysiological and neuroimaging methods to provide information about the physiological dynamics of cognitive reserve.*
Materials and Methods*: The aim of this research was to study the relationship between cognitive reserve and absolute power (AP) of the electroencephalogram (EEG) registered during the Wisconsin Card Sorting Test (WCST) of older adults without neuropathology. The EEG of 10 healthy elderly people was recorded during WCST solution, CR was measured and correlated with the AP of the EEG.*
Results*: Cognitive reserve was negatively associated with the AP of the Delta and Theta bands. It was also found that there are descriptive differences in the magnitude of AP according to the level of CR, suggesting a differentiating effect of CR on EEG dynamics.*
Conclusion: *CR is negatively correlated with AP, this implies that the participants with low CR may have less efficient task-related brain dynamics.*
Key Word*: Cognitive Reserve, Electroencephalography, Aged, Wisconsin Card Sorting Test, Neurophysiology*

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I. Introduction

Cognitive reserve (CR) is a neuroprotective factor that allows the person to modulate cognitive impairment or mitigate the impact of negative conditions such as dementias. This mitigation is achieved through the recruitment or optimization of alternative neural networks for the execution of the affected cognitive processes[1,2,3,4]. Cognitive reserve is developed throughout life and is usually measured from proximal variables such as educational level, IQ, occupational complexity, participation in stimulating cognitive activities, leisure activities, lifestyle, physical activity, exercise, and social interactions[2,5,6,7].

Neurophysiological techniques such as electroencephalography allow the analysis of neuronal activity and facilitate the observation of the functional dynamics of cognitive processes and how they are influenced by factors such as cognitive reserve, whose effect on EEG power must still be described in depth. Recently, research models have been designed to study cognitive reserve using neurophysiological and neuroimaging methods[7]. These models allow the design of experimental protocols to provide information about the physiological dynamics of cognitive reserve; using as a basis the transversal model proposed by Stern[7], and the neuronal efficiency models proposed by Steffener and Stern[8], this research aims to describe the effects of cognitive reserve on the absolute power of the electroencephalogram recorded during a task of executive functions in healthy elderly participants in order to assess three questions: 1) What is the relation between cognitive reserve and absolute power of the EEG frequency bands during cognitive processing? 2) Which frequency spectrum of the EEG is more sensitive to the different levels of cognitive reserve? 3) Are the patterns of absolute power dependent of the level of cognitive reserve?

Therefore, the aim of the research was to study the relationship between cognitive reserve and the absolute power of the electroencephalogram of older adults registered during a task of executive functions. It was hypothesized that older adults with higher cognitive reserve will have more efficient cortical activation patterns in response to the demands of a cognitive task, so that their electroencephalogram will show lower absolute power in delta and theta bands.

II. Material And Methods

We carried out a quasi-experimental prospective study, during a period of 12 months (from January 2018 to December 2018), considering cognitive reserve as an independent variable, and absolute power as a dependent variable. A non-probabilistic sampling was carried out by volunteering in which 26 adults over 60 years old participated, 16 were excluded due to history of depression, anxiety, diagnosis of Alzheimer's disease or dementia, or for presenting cognitive impairment measured with the Mini-Mental State Examination[9]. The final study sample consisted of 10 old adults without neuropathology (see Table 1. For sample description).

Table 1. Description of the study sample (n = 10)

	Mean ± SD
Age	68.2 ± 7
Years of schooling	10 ± 6
Occupational complexity	5 ± 3
Monthly income*	7150 ± 5543 (354 ± 274)[2]
Mini Mental Score	29 ± 1.2
WCST[1] completed categories	2 ± 1
Cognitive Reserve Index	0.41 ± 0.10

*Amount in mexican pesos; [1]Wisconsin Card Sorting Test;
[2]amount in American dollars

Ethics

This research protocol has been approved by the *Comité de Ética en Investigación de la Facultad de Psicología-Xalapa* (CEI-FP) (CONBIOETICA30CEI00820150409) with registration number CEI-FP/008/2017, this committee has verified that the research complies with the criteria necessary to be considered as risk-free for the participants and has granted the researchers an approval to perform it in the period between January 9, 2018 and January 9, 2019.

Procedure

To measure the cognitive reserve a Cognitive Reserve Index (CRI) was calculated using a cognitive reserve instrument that consists of 39 indicators of cognitively stimulating activities in which the participants must identify how many days per week they perform the activity, the maximum score of the instrument is 273, this instrument is still in validation process; the years of schooling completed by the participant are added to this value, the maximum score in the education category is 21 (considering 2 years for master's degree and 3 for PhD in Mexico’s educational system); in addition, the occupational complexity score is added, this is obtained from the National Classification System of Occupations (SINCO)[10]. Which is a tool that is used to reflect the occupational structure of Mexico, granting a value according to the salary and complexity of any given occupation, however, for this index, the original scale was inverted so that the score of the least complex occupation score corresponded to 1 and the score of the most complex occupation score to 9 (previously 9 and 1 respectively).

The formula used to calculate the Cognitive Reserve Index was:

$$\text{CRI} = \frac{CR\ score + \text{Years of schooling} + \text{Occupational complexity}}{303}$$

Where the *CR Score* is the score obtained by the participant in the cognitive reserve instrument and 303 is the total score that can be obtained by adding the three components of the Index. The result of the calculation is a value between 0 and 1 where higher scores indicate that the participant has more indicators that favor cognitive reserve, this score was used as a proxy measure of the level of cognitive reserve for each participant.

The electroencephalogram (EEG) was recorded in the mornings between 09:00 and 11:59 a.m. in a cubicle with dim light, free of distracting stimuli and electrically isolated. It was recorded with the software Curry Neuroimaging Suit 7.0.10 XS Neuroscan System with 32 Au (gold) electrodes placed according to the International 10-20 System on the scalp in the leads: FP1-FP2, F7-F8, F3-F4, Fz, FT7-FT8, FC3-FC4, FCz, T7-T8, C3-C4, Cz, TP7-TP8, CP3-CP4, CPz, P7-P8, P3-P4, Pz, O1-O2, and Oz. Two references were placed on the mastoid bones behind the ears (M1 and M2) and a ground electrode (GND) on the forehead of the participant. Four electrodes were placed to control the eye movements (VE1, VE2, HO1 and HO2). Cardiac activity was recorded by means of two electrodes located below the clavicles (EKG1 and EKG2). The recording parameters of the electroencephalogram were: Sampling frequency at 1 kHz, High Pass Filter at 0.5 Hz, Low Pass Filter at 30 Hz, Notch Filter at 60 Hz with harmonics, artifact reduction with threshold Lower at -200 μV and Upper at 200 μV.

A clinical EEG protocol (eyes-closed, eyes-open, hyperventilation, recovery of hyperventilation, photostimulation and auditory stimulation) was used to analyze the brain's electrical activity with the purpose of determining if the participant's activity was within the expected for his age and exclude cases that present paroxysmal activity. The basal EEG activity of each participant was characterized by the frequency and amplitude predominant in occipital regions. The symmetry and interhemispheric synchrony were analyzed, the segments corresponding to eyes-closed and eyes-open were extracted from the clinical protocol for its consideration as resting state basal activity. In order to demonstrate the effect of cognitive reserve, and to assess its impact on the neurophysiological dynamics associated with cognitive processing, after the clinical EEG protocol, and still during the EEG, the participants performed the Wisconsin Card Sorting Test (WCST) on a computerized version of the STIM2 software v4.0 Neuroscan. This test was selected because cognitive reserve is highly dependent on the complexity of the cognitive tasks that the person faces, and also favors the integration of neural networks to meet the demands of a cognitive task, since the executive functions are one of the cognitive processes that are most affected in aging, and that they also require the recruitment of brain areas associated with language, memory and other cognitive processes, it was considered that the execution of a task of executive functions would be cognitively demanding for the aged participants and that it would allow us to inquire the effect of the cognitive reserve.

For the preprocessing of the signal, the EEG was re-referenced to the common average reference (CAR), later, in the software Neuroscan v4.5 of Compumedics USA, Inc. The full EEG recording was segmented in 5 conditions (eyes-closed-basal, eyes-opened-basal, and WCST minutes 0 to 3, WCST minutes 3 to 6 and WCST minutes 6 to 9) in epochs of one second (1024 sampling points) which were submitted to visual inspection by a single researcher to identify and eliminate the segments that presented artefacts. Absolute power was then calculated from the epochs, the Neuroscan Averaging module was used to calculate the power spectrum through the Fast Fourier Transform, using the parameters: Welch window function at 10%, resolution 0.978 Hz, duration 1023 ms, 500 Hz range, 1024 sampling points.

The Absolute Power of each frequency band for each of the electrodes was averaged in twelve analysis areas: Left Side (F7, FT7, T7, TP7, P7), Medial Left (FP1, F3, FC3, C3, CP3 , P3, O1), Central Line (FZ, FCZ, CZ, CPZ, PZ, OZ), Medial Right (FP2, F4, FC4, C4, CP4, P4, O2), Right Side (F8, FT8, T8, TP8 , P8), Anterior Left (FP1, F7, F3, FT7, FC3), Anterior Right (FP2, F8, F4, FT8, FC4), Posterior Left (TP7, CP3, P7, P3, O1), Posterior Right (TP8, CP4, P8, P4, O2), Central Left (T7, C3), Central Right (T8, C4), and Parieto-Occipital (P3, PZ, P4, O1, OZ, O2).

Statistical analysis

To analyze the relationship of between cognitive reserve and absolute power (AP) of the EEG, the Spearman correlation analysis was used, correlation tests were performed with a unilateral hypothesis contrast. To compare the AP of delta, theta, alpha and beta bands corresponding to each of the 5 conditions of the EEG (eyes-closed-basal, eyes-opened-basal, and WCST minutes 0 to 3, WCST minutes 3 to 6 and WCST minutes 6 to 9), Generalized Linear Models (GLM) of repeated measures were used with intrasubject contrasts, in case of violation of the sphericity assumption in the repeated measures analysis the Greenhouse-Geisser adjustment was carried out. To identify and describe the patterns of AP according to cognitive reserve level, a hierarchical cluster analysis with a single solution (3 groups) was used to divide the sample in 3 levels (low, medium, and high) of cognitive reserve. Profile line plots were used for each cognitive reserve group considering the 5 EEG conditions of analysis (baseline and experimental), to assess the differences at a descriptive level between the increments in AP when passing from the eyes-open condition to the WCST according to the CR level, a subtraction was carried out were the AP of the eyes-opened-basal condition was subtracted from the AP of each of the three WCST conditions, these values were compared with ANOVAs after verifying the assumptions with Shapiro-Wilk and Levene's tests and Bonferroni corrected for multiple comparisons.

III. Result

We found negative correlations between the Cognitive Reserve Index (CRI) and the absolute power (AP) of the delta and theta frequency bands in the basal conditions of eyes-closed-basal and eyes-opened-basal (Table 2).

Table 2. Significant correlations between Cognitive Reserve Index and Absolute Power.

	Eyes Closed				**Eyes Opened**	
	Delta		**Theta**		**Delta**	
Area	r_s	p	r_s	p	r_s	p
Medial left	-.685	0.014	-.612	0.030	-.709	0.011
Central line	-.552	0.049	-.564	0.035		
Anterior left			-.661	0.019		
Posterior left	-.624	0.027	-.685	0.014	-.673	0.017
Parieto-Occipital	-.624	0.027	-.553	0.049	-.552	0.049
Anterior right					-.552	0.049
Central left					-.612	0.030

r_s = Spearman's Rho

In the 0-3 minutes of the WCST analysis, negative correlations of the CRI were found with the AP of the Delta band in the areas: Medial Left (Spearman's rho [r_s] = -.673, p = 0.017), and Left Posterior (r_s = -.697, p = 0.013); with the AP of the Theta band in the areas: Medial Left (r_s = -.685, p = 0.014), Anterior Left (r_s = -.564, p = 0.045), Left Posterior (r_s = -.624, p = 0.027), and left Central (r_s = -.564, p = 0.045); and with the AP of the Beta band in the medial Left area (r_s = -.612, p = 0.030).

In the 3 to 6 minutes of the WCST analysis, negative correlations of the CRI with the AP of the Delta band were found in the areas: Medial left (r_s = -.564, p = 0.045), Left posterior (r_s = -.697, p = 0.013), Central left (r_s = -.552, p = 0.049) and Parieto-Occipital (r_s = -.552, p = 0.049); with the AP of the Theta band in the areas: Left side (r_s = -.612, p = 0.030), Medial left (r_s = -.648, p = 0.021), Left posterior (r_s = -.648, p = 0.021), Central left (r_s = -.624, p = 0.027) and Parieto-Occipital (r_s = -.588, p = 0.037); and with the AP of the Alpha band in the areas: Medial Left (r_s = -.661, P = 0.019), Left Posterior (r_s = -.564, p = 0.045) and Parieto-Occipital (r_s = -.588, p = 0.037).

In the 6 to 9 minutes of the WCST analysis, negative correlations of the CRI were found with the AP of the Delta band in the areas: Left side (r_s = -.564, p = 0.045), Medial left (r_s = -.697, p = 0.013), Central line (r_s = -.636, p = 0.024), Left posterior (r_s = -.661, p = 0.019), Central left (r_s = -.588, p = 0.037) and Parieto-Occipital (r_s = -.697, p = 0.013); with the AP of the Theta band in the following areas: Central line (r_s = -.564, p = 0.045) and Parieto-Occipital (r_s = -.564, p = 0.045); with the AP of the Alpha band in the areas: Medial Left (r_s = -.648, p = 0.021), Anterior Left (r_s = -.552, p = 0.049), Left Posterior (r_s = -.600, p = 0.033) and Parieto-Occipital (r_s = -.588, p = 0.037); in all three bands, absolute power was lower in the participants with more cognitive reserve. Figure 1 shows the correlated electrodes and areas for each frequency band.

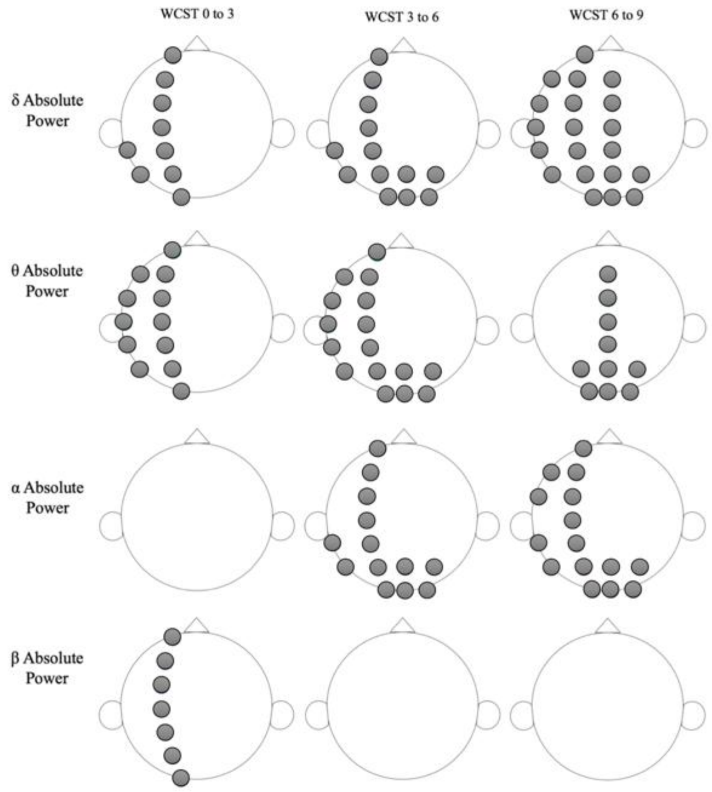

Figure 1. Correlated areas between the CRI and the absolute power of each frequency band during the three WCST conditions.

The GLM results showed that the AP of the Delta and Theta bands changed through the five conditions in all EEG areas (Table 3), regarding the alpha band the WCST increased the AP in the right side (F = 7.02, df = 1.290, p = 0.017), anterior right (F = 6.546, df = 1.066, p = 0.028) and posterior right (F = 4.968, df = 1.134, p = 0.046). No increments were found in the Beta band.

Table 3. GLM results of Delta and Theta bands

	Delta				Theta			
Area	**SS**	**df**	**F**	**p**	**SS**	**df**	**F**	**p**
Left side	14.519	1.425 G	31.025	< 0.001	1.962	1.991 G	27.312	< 0.001
Medial left	21.858	1.511 G	23.475	< 0.001	4.653	1.739 G	27.727	< 0.001
Central line	2.279	1.329 G	16.215	0.001	1.130	1.301 G	18.781	0.001
Medial right	9.745	1.934 G	41.436	< 0.001	2.909	1.789 G	25.009	< 0.001
Right side	35.062	1.212 G	21.792	< 0.001	4.544	1.782 G	30.234	< 0.001
Anterior left	72.841	1.243 G	16.311	0.001	9.999	1.667 G	19.764	< 0.001
Anterior right	39.973	1.265 G	24.951	< 0.001	5.859	1.575 G	31.918	< 0.001
Posterior left	5.839	4	47.741	< 0.001	2.150	1.783 G	20.663	< 0.001
Posterior right	9.539	1.481 G	34.061	< 0.001	2.577	1.758 G	25.514	< 0.001
Central left	7.127	1.375 G	23.815	< 0.001	0.750	4	31.278	< 0.001
Central right	9.884	1.350 G	16.765	0.001	1.468	1.537 G	17.648	< 0.001
Parieto-Occipital	9.750	4	38.333	< 0.001	5.452	1.528 G	21.195	< 0.001

SS = Sum of squares, df = degrees of freedom, G = Greenhouse-Geisser correction

The increments in AP according to the CR level showed a similar pattern in all the registered EEG areas for the delta and theta bands, in this pattern the low CR group had more AP than the other two groups, however when comparing the AP increments from the eyes-opened-basal condition to each of the WCST conditions between groups only two statistical differences were found, for the delta band, increments in AP were different between the CR levels ($F_{2,7} = 6.01$, $p = 0.03$) in the parieto-occipital area (Figure 2), the post-hoc analysis showed that the low CR group had more AP than the medium CR group (mean difference: 0.737 μ^2) in the WCST 6 to 9 minutes condition, for the theta band the difference was found in the medial left area ($F_{2,7} = 4.810$, $p = 0.048$), the post-hoc analysis showed that the low CR group had more AP than the high CR group (mean difference: 0.729 μ^2) in the WCST 3 to 6 minutes condition (Figure 3).

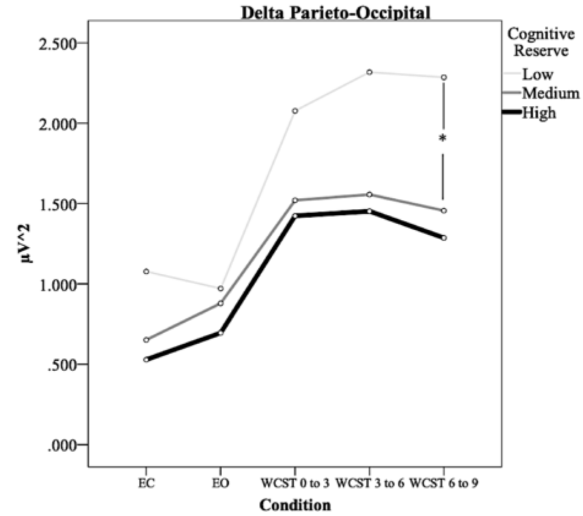

Figure 2. Absolute power increments of the delta band in the parieto-occipital area according to the cognitive reserve level. The dots correspond to the mean AP for each group. EC = Eyes-closed-basal, EO = Eyes-opened-basal, WCST = Wisconsin Card Sorting Test.

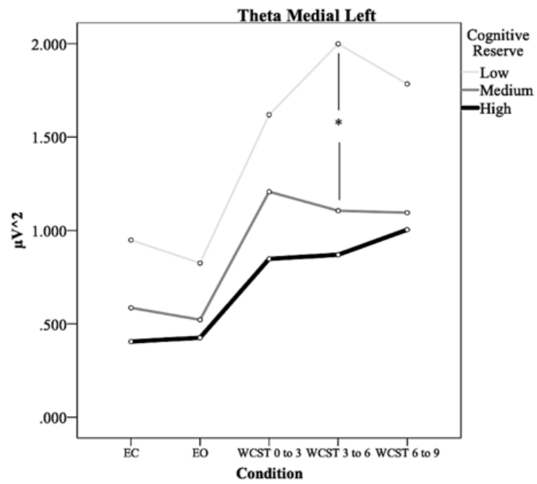

Figure 3. Absolute power increments of the theta band in the medial left area according to the cognitive reserve level. The dots correspond to the mean AP for each group. EC = Eyes-closed-basal, EO = Eyes-opened-basal, WCST = Wisconsin Card Sorting Test.

IV. Discussion

This study was conducted to examine the relationship between cognitive reserve (CR) and absolute power (AP) of the EEG registered during a task of executive functions in healthy older adults. Next, we discuss how our results relate to prior literature, offer an interpretation of the observed relationships, describe the limitations and outline future research lines to consider.

In contrast to what is reported by other authors[11,12], no differences were found between the basal conditions of eyes-closed and eyes-opened in the delta and theta bands, where effects of the cognitive task and cognitive reserve were observed, nonetheless we agree with the mentioned authors regarding the importance of using different baseline conditions (EO or EC) depending on the type of task that participants carry out, where the eyes-opened condition is more appropriate for cognitive and visual tasks, like the one used in this research.

We found negative correlations between CR and AP at all the EEG conditions, the associations were more numerous for the slow EEG bands delta and theta, therefore, we believe that slow EEG bands are more sensitive to CR. In previous research the increments in theta band have been described as a possible biomarker of cognitive aging in patients with mild cognitive impairment and dementia[13,14], the negative correlation between CR and AP of the Theta band found in this research could be showing the neuroprotective effect of the cognitive reserve, this is because the participants with greater cognitive reserve had lower absolute power in the delta and theta bands, however, we still need to investigate in depth the effect of the cognitive reserve on the brain electrical activity recorded at resting states.

During the WCST conditions, negative correlations were found between the CR and the AP of the slow bands delta, theta and also with the Alpha band, this EEG bands are related to cognitive processes such as focused attention, mental calculation and concentration[15], it has been theorized that theta band recorded during cognitive tasks, reflects the effect of more general processes of attention and cognitive control[16], and its function at a neurophysiological level is the integration of different brain structures such as the hippocampus, the medial temporal cortex and different areas of the neocortex in neurocognitive networks for cognitive processing[17,18,19], the correlation between CR and EEG AP with these bands may be reflecting the recruitment of additional networks and neuronal areas to meet the cognitive demands of the task of executive functions.

In the graphic analysis it was shown that there are descriptive differences in the magnitude of AP according to the level of CR, suggesting an effect of CR on AP, this finding could indicate that the neural networks of the participants with less cognitive reserve are less efficient according to the model of neuronal activity associated with cognitive tasks proposed by Steffener and Stern[8], these results are similar to those reported by other authors[20] who with magnetoencephalography recorded brain activity of healthy older adults while performing a memory task and found that participants with less cognitive reserve had greater functional connectivity than those with more cognitive reserve; this findings support the proposed hypothesis that the brain electrical activity of high CR persons will be more efficient and that this effect can be observed in the delta and theta bands.

The increases in AP in the delta and theta bands at the WCST conditions allowed us to confirm that cognitive processing requires greater synchronization of brain electrical activity, this result is consistent with previous research that also found increases in AP of the theta band when passing from a basal condition to the WCST solution[21] the increment in this band is considered to reflect the recruitment of the working memory process necessary for the solution of the WCST, specifically the increases observed in the AP of the theta band in the left hemisphere in temporal, parietal and occipital areas, could be associated with the role that this activity has in the recovery and coding of the memory process necessary for the WCST solution, along the same lines, it has been described that the oscillations of the theta band are dependent on cognitive tasks, both for spatial processing and for working memory[22].

The synchronization of the oscillations of the theta band has been associated with the effect of cognitive processing exerted by the prefrontal cortex in the parietal and temporal regions which allows the maintenance of information in working memory[23,24], this effect is observable through the WCST, since this task requires several cognitive processes for its solution and these processes have a different time of action, at the beginning of the task the participant must use language and long-term memory to be able to identify and name the categories necessary to solve the test, in this phase mainly occipital, temporal and parietal areas are recruited; in the middle of the task the participant must start to run the test and through feedback generate multiple possible ways of solving the task, this phase requires working memory and attention, processes that are associated with temporal and prefrontal areas; at the end of the task, when the solution rules have already been learned, the participant must keep them in mind during their execution and be attentive to the feedback stimuli that indicate category changes; so the execution in this phase occurs mainly in prefrontal areas; therefore, the WCST favors the neurophysiological observation of different cognitive processes and their association with CR could be mediated by the mechanism of recruitment of different neural networks, the variations in the number of correlations found for each segment of the WCST may indicate that depending on the time segment analyzed the effects of cognitive processing can be observed in different frequency bands.

This research provides exploratory evidence about the neurofunctional dynamics of CR studied with electroencephalography. We found a subtle effect and negative correlations between CR and AP of the EEG of healthy older adults, showing that low CR implies less efficient task related activation, it was also found that the EEG registered during cognitively demanding tasks is useful to demonstrate the effect of CR on brain dynamics.

Limitations

Among the limitations of the research is the small sample size, this limitation could be mediated by the comorbidity of diseases in aging making difficult to gather cognitively healthy old adults, and therefore the size of the groups for each level of cognitive reserve is also small, however, we expect that the effect of the cognitive reserve observed in the absolute power increments, could be replicated in a larger sample. Another methodological limitation is that a minimum knowledge about how to use a computer is required for the solution of the computerized WCST so that participants with low educational levels or without previous experience are at a disadvantage, using the traditional version of the WCST could solve this problem, however, synchronization with the EEG equipment would be lost.

Future research

Subsequent research should analyze the effect of cognitive reserve in the other quantitative EEG measures, specifically the electroencephalographic coherence should be studied given its functional correlation with the cognitive reserve theory.

V. Conclusion

Cognitive reserve is negatively correlated with the absolute power of the Delta and Theta bands recorded during cognition. Delta and Theta frequency bands are the most sensitive to the effect of cognitive reserve and this effect is observed mainly in areas of the left hemisphere. Executive functions require greater synchronization of absolute power in the Delta and Theta bands compared to the basal resting activity of eyes-closed and eyes-opened. The absolute power was not statistically different depending on the level of cognitive reserve, however, at descriptive level a pattern is observed in which older adults with more cognitive reserve show consistently less AP compared to those with lower cognitive reserve when solving the Wisconsin Card Sorting Test.

Declaration of conflicts of interest

The authors declare that in this study, there are no relevant conflicts of interest.

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