



Physical, Cognitive and Environmental Factors in Patients with Moderate and Severe Cognitive Decline. Analysis of Specific Neuropsychological Measures and Frequency EEG Bands

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Citation: Fabio RA, Gangemi A, Nocera F, Cardile S (2018) Physical, Cognitive and Environmental Factors in Patients with Moderate and Severe Cognitive Decline. Analysis of Specific Neuropsychological Measures and Frequency EEG Bands. J Psychiatry Cogn Behav: JPCB-146. DOI: 10.29011/2574-7762. 000046

Received Date: 01 September 2018; **Accepted Date:** 05 October 2018; **Published Date:** 15 October 2018

Abstract

Background: Cognitive decline is the result of a combination of different factors; although the presence of non-modifiable risk factors, there are physical, cognitive and environmental factors, potentially-modifiable, that influence the development of the disease and that therefore represent a potential to reduce the incidence of cognitive decline. Although many studies have focused on factors affecting the onset of cognitive decline; the aim of the present study is to analyse which specific risk factors influence specific cognitive domains examined through the MoCA neuropsychological test. The second aim is to analyse if these risk factors would also compromise the functioning of alpha and beta band EEG measurements.

Methods: The sample analysed for this study included fifty subjects affected by mild cognitive impairment or major neurocognitive diseases (MMSE score between 12 and 24) and 50 healthy participants. All participants were subjected to neurological consultation, an EEG test, and the MoCA neuropsychological test and “CSHA Risk Factor Questionnaire” were administered.

Results: Level of education, qualification achieved, practicing or having regularly practiced physical, leisure or mental leisure activities, engaging in regular exercise, excessive smoking or the presence of specific physical, psychological or psychiatric conditions such as stomach ulcer, stroke, epilepsy, the presence of paralysis of some kind, learning difficulties and depression were all associated in some measure with cognitive decline and have an impact both on MoCA global scores and, in a different way, on the subscales of the latter. Other predisposing factors (like diabetes, thyroid disorders) correlated only with the individual subscales of MoCA but not with the global MoCA. With regard to frequency EEG bands, the experimental group showed significantly lower levels of alpha and beta values than the control group. No significant correlations were found whereas predisposing factors affected neurophysiological measures.

Conclusions: Significant correlations between performance in each subscale of the MoCA neuropsychological test and some lifestyle factors, past or current, were revealed. Furthermore, also regarding neurophysiological measurements, in alpha and beta band EEG measurements, significant differences were recorded between subjects with cognitive decline and healthy subjects.

Keywords: Cognitive Decline; MoCA Test; Risk Factors

Introduction

Cognitive decline is a condition that is gaining importance due to the increase of incidence worldwide. Life expectancy increase in the last decade has brought with it an increase in the number of individuals affected by dementia. In addition to the dev-

astating consequences that this condition has on the individuals affected and their families, the elevated number of patients affected by dementia represents a huge concern at social and economic levels for society and healthcare systems [1].

Cognitive decline is represented by a significant change in cognitive performances from a premorbid baseline level [2,3]. These performances include different cognitive domains such

as memory, attention, executive functions, perception, language and psychomotor functions [4]. It is the result of a combination of different factors that include: age, gender, genetic factors, inflammation, co-morbidity, environment and lifestyle factors [5]. Although age, gender and specific genetic predispositions are the major non-modifiable risk factors, there are other potentially-modifiable factors that have been linked to the development of the disease and that therefore represent a potential to reduce the incidence of cognitive decline [6-9]. In particular, some studies indicate that cardiovascular risk factors (e.g. hypertension, diabetes, cerebrovascular diseases, obesity, metabolic syndrome), lifestyle factors (e.g. unhealthy diet, smoking, high alcohol consumption, reduced social and physical cognitive activity, chronic stress) and psychosocial factors (e.g. lack of a rich social connection, depressive symptoms) have an impact on the risk of developing Alzheimer's and other forms of dementia [10-12].

From a neuroanatomical perspective, it has been found that cognitive activities and socially demanding activities can increase the number of synaptic interconnections between nerve cells and reduce the percentage of hippocampal atrophy compared to individuals with lower levels of activity [13,14]. A number of leisure activities such as reading, playing board games, playing an instrument or dancing have been associated with a reduced risk of cognitive decline as well [15]. Bilingualism has also been associated with a delayed onset of cognitive decline, independent from levels of education, and can therefore specifically protect against attention and executive functioning decline [16]. Indeed, physical activity seems to increase the Brain-Derived Neurotrophic Factor (BDNF) that promotes the growth, functioning and longevity of neurons [17], as well as non-neuronal factors of the brain, such as vascularization [18]. It has been observed that individuals that perform physical activity on a daily base have a reduced incidence of cognitive decline compared to individuals that perform physical activity occasionally [19]. A healthy diet, such as the Mediterranean diet, rich in antioxidants, vitamins (e.g. vitamin B₁₂, E and D) and polyunsaturated fatty acids (e.g. omega-3) can reduce the risk of cognitive decline by reducing, for example, the risk of cardiovascular diseases [20,21]. Smoking has been associated with an increased risk of cognitive decline as well [22]. However, some studies observed an apparent protective effect of smoking given by the observed cholinergic action of nicotine against Parkinson's disease [23]. A moderate consumption of alcohol seems to protect elderly individuals from cognitive decline, in particular from Alzheimer's disease [24,25]. Nevertheless, some studies demonstrated that heavy alcohol consumption could be associated with an increased risk of cognitive decline, especially in patients with mild cognitive impairment or individuals that carry the APOEε4 allele [26, 27].

Cardiovascular diseases are increasingly recognised not only as a risk factor for vascular dementia but also for neurodegenerative

dementia, in particular, Alzheimer's disease [28]. Hypertension, high cholesterol, high Body Mass Index (BMI) and diabetes mellitus are all factors associated with an increase in the risk of cognitive decline in older age [29,30]. Head injuries have been also associated with a higher risk of cognitive decline and the severity of the injuries seems to increase the risk of incidence of the latter [31]. A number of approaching and cross-sectional studies explored the relationship between Electroencephalogram (EEG) and cognitive decline with the aim of identifying markers of cognitive decline and dementia [32-37]. In line with this prospective, different studies examined EEG correlates of global cognition, mostly using compound tests such as the Mini-Mental State Examination (MMSE) [38], Global Deterioration Scale [39] or Cambridge Cognitive Examination [40] [34].

Cross-sectional investigations in elder individuals affected by different levels of cognitive impairment have reported associations between EEG spectral parameters, i.e. higher theta activity during rest and lower alpha activity during memory activation, and decreased MMSE [33,41]. An exploratory study [34] tested whether the EEG power and coherence measurements in subjects characterized by a cognitive spectrum ranging from the elderly without cognitive problems to those with Alzheimer's were related to specific cognitive domains including global cognition, memory, language and executive functioning. They observed that EEG power measurements were associated with decreased performance on tests of global cognition, memory, language and executive functioning, while coherence measures were not considered [34].

Although many studies focused on the factors affecting the onset of cognitive decline, the contribution of the present study is broader; the aim is to analyze which specific risk factors influence specific cognitive domains examined through the Montreal Cognitive Assessment (MoCA) neuropsychological test (visuospatial/executive, naming, memory, attention, language, abstraction, delayed recall and spatial-temporal orientation). The second aim is to analyze if these risk factors would also compromise the functioning of alpha and beta band EEG measurements.

Materials and Methods

Participants

The sample analyzed for this study included 100 subjects, aged from 45 to 95 (SD= 13.12). Fifty tested subjects show Mild Cognitive Impairment (MCI) or major neurocognitive diseases such as Alzheimer's disease, vascular dementia, Parkinson's disease or other pathological conditions accompanied by cognitive decline, such as Temporal Lobe Epilepsy (TLE), while, the remaining 50 patients were healthy, gender and age matched, not presenting any form of MCI or major neurocognitive disease.

With regard to the experimental sample, the subjects that took part in the research were subjected to neurological consultation

and EEG tests and only patients with an MMSE score between 12 and 24 (the MMSE score was adjusted to the level of education of the participants) were included. All the subjects involved in this study participated voluntarily and gave their informed consent before participation.

Subjects Experimental Group	Age (Years)	Gender	Education (Years)	MMSE	Duration of Disease (Years)
1	81	F	5	18.4	15
2	65	F	8	18	4
3	72	F	6	21.7	7
4	86	F	5	20.4	18
5	87	F	5	13.4	10
6	62	M	8	23	3
7	76	M	5	17.7	16
8	55	M	13	23	2
9	68	M	5	15.9	10
10	78	F	8	15	16
11	81	F	3	20.5	6
12	54	F	5	20	2
13	81	F	13	22.1	5
14	71	M	8	21.4	10
15	79	F	0	15.5	13
16	62	M	5	24	1
17	82	F	4	21	14
18	61	F	13	24	1
19	75	M	6	23.3	4
20	76	F	4	22	6
21	45	F	8	22	3
22	71	F	16	17.7	8
23	76	F	5	19.7	7
24	51	F	12	24	2

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25	50	M	8	19	3
26	85	F	2	23.2	6
27	79	M	5	18.7	18
28	57	M	13	24	2
29	65	F	8	23	3
30	50	M	11	21	1
31	72	M	8	19.4	1
32	69	F	8	16	6
33	51	M	13	22	2
34	84	F	0	15.5	20
35	92	M	5	14	25
36	21	M	8	23	2
39	46	F	8	21	4
40	76	F	13	22.7	8
41	47	F	5	23	2
42	63	F	5	20	3
43	87	M	8	15.8	16
44	86	M	5	23.4	6
45	60	M	1	17	3
46	61	F	5	18	2
47	46	F	13	23	4
48	71	F	6	20	8
49	47	F	8	22	1
50	50	M	0	19	2

Subjects Control Group	Age (Years)	Gender	Education (Years)	MMSE
1	83	F	13	28.1
2	72	M	12	27.4
3	62	F	5	27
4	51	F	13	29
5	80	F	8	25.7
6	57	M	8	29
7	76	F	5	26.7
8	62	F	5	29
9	50	M	10	29
10	50	M	13	29
11	54	F	13	29
12	48	F	13	29
13	70	F	5	28.3
14	85	F	10	26.8
15	71	F	12	26.3
16	70	F	5	27.3
17	76	M	5	26
18	76	F	12	26
19	76	F	8	25.7
20	47	F	7	29
21	60	M	13	28
22	51	M	8	29
23	86	M	13	28.8
24	72	F	8	26.3
25	64	F	5	29
26	46	F	15	29
27	45	F	13	28
28	65	F	13	26.2
29	62	M	13	29.3
30	87	F	13	28
31	55	M	14	28
32	75	M	13	26.7
33	87	M	13	29.3

34	77	M	13	27.3
35	79	M	8	28
36	90	M	13	29.3
37	69	F	13	26.2
38	50	M	16	29
39	68	F	13	26.02
40	67	M	5	29.4
41	69	F	5	29.4
42	68	M	2	28.4
43	84	F	8	28.7
44	80	F	5	29.4
45	82	F	13	28.1
46	46	F	13	29
47	62	M	8	28
48	78	F	13	27.3
49	86	F	13	27.3
50	65	F	13	26.2

Table 1: Shows clinical and demographic characteristics of experimental group subjects and control group subjects.

Materials

Neuropsychological Measures

Mini-Mental State Examination (MMSE) [38]

The MMSE is a brief, rapid test of cognitive impairment that includes 30 items grouped into five categories: orientation, registration, attention and calculation, recall and language. The test is divided into two sections; the first requires verbal responses to orientation, memory and attention questions. The second requires naming, reading and writing and the ability to follow verbal and written commands, write a sentence and copy a polygon [42]. This test requires 10-15 minutes more or less for administration and the final score is between 0 and 30 points. The most widely used cutoff is a score of less than 24. The test has been subjected to clinical validation and has been calibrated for the elderly individuals taking into account both the age and the socio-educational level for which correction coefficients have been created [43].

Montreal Cognitive Assessment (MoCA) [44]

MoCA is a screening test used to evaluate cognitive functions of the subject in a short time, 15 minutes more or less. The test is divided into ten domains: visuospatial/executive function,

naming, forward and backward digit span, target detection task, serial subtraction task, repetition of sentences, language fluency, abstraction, memory, orientation. Visuospatial abilities are assessed using a clock drawing task and copying a three-dimensional cube. Executive functions are assessed using an alternation task drawing a line from a number to a letter in ascending order. Naming is assessed using three animals (lion, camel, rhinoceros). By repeating a list of digits in forward and backwards order, a target detection task, as well as a serial subtraction task, attention abilities are evaluated. Language is assessed through repetition of two syntactically complex sentences and a fluency task. Abstraction is evaluated using a similarity task [42].

The maximum obtainable score is 30 and a score of 26 or above is considered normal. For the evaluation of the final score, it is necessary to consider the level of education of the subject, adding 1 point if the total period of education is lower or equal to 12 years. The test has been translated and calibrated in different languages. For our research, the Italian version was used.

EEG Registration

An Electroencephalogram (EEG) is defined as the electrical activity of an alternating type recorded from the scalp surface after being picked up by metal electrodes and conductive media [45]. The EEG data were acquired using a gold-standard digital EEG amplifier (Cardinal Medical System). The system continuously recorded EEG signals over 19 channels. The electrodes were placed using the criteria of the International Measurement System 10/20, on the frontal-temporal area. Brain waves have been categorized into four basic groups: beta (>13 Hz), alpha (8-13 Hz), theta (4-8 Hz), delta (0.5-4 Hz).

To analyze EEG data, Quantitative EEG (QEEG) were used. It applies multi-channel measurements that can better determine spatial structures and localize areas with brain activity or abnormality. The collected data is transformed into frequency domains using computerized algorithms and scalp map of different frequency bands is then obtained.

Risk factors Assessment

To detect the lifestyle factors and the other possible predisposing factors to cognitive decline, we used the “CSHA-Risk Factors Questionnaire”, translated in Italian (Canadian Study of Health and Aging, 2002) [46]. It is a questionnaire composed of 46 items that allow the evaluation of risk factors analyzing the following domains: personal life history (date and place of birth, marital status, education, ethnic origins), institutional and occupational history of the subject, hobbies and sports performed by the subject, exposure to particular substances in the workplace or during leisure time, context of the subject’s family life, current and past physical and psychiatric/psychological condition of the

subject, use of particular drugs or exposure to vaccines and, finally, subject’s lifestyle (alcohol consumption, smoking, nutrition, current physical activity). Since cognitive deficit can impede patients from providing accurate information, the questionnaire can be administered to relatives (a spouse, a son/daughter) that know the patient very well.

Procedure

Prior to administration of the tests, the objective of the research was explained to the subjects who were then asked to complete and sign a consent form. Concerning the administration, each test was administered by means of an assistant: each question was read, explained and explicated to the subject, who then answered following the given guidelines. All the answers were then recorded by the assistant, except for the tests evaluating cognitive abilities in which the subject had to write, draw or copy some figures by his own hand.

The administration of the CSHA test took more time than predicted, about 20-25 minutes, compared to the two tests, MoCA and MMSE, that instead took approximately 15 minutes each. Following the test administration, the possibility was given to the subjects to ask any questions and to resolve any doubts they may have had; the patients were then thanked for their participation in the study. Furthermore, at the end of the administration of the tests, the overall scores of the MoCA and MMSE tests were calculated, keeping in mind to make the appropriate corrections in relation to the years of education of each subject.

Statistical Analyses

For statistical analysis, the IBM SPSS version 22 software (IBM, Armonk, NY, USA) was used. Level of significance was set at $\alpha = 0.05$. The Kolmogorov–Smirnov test ascertained normal distribution of data. First, differences in task performance as indexed by correct responses in MoCA (and the related subscales) between the groups (patients with cognitive decline and control subjects) was analysed. Repeated-measures-ANOVAs (RM-ANOVA) (between-subject factor “Group”, within-subject factors: Subscales of MoCA) were performed to detect the effects of group on dependent variables of both MoCA test and subtests.

The association between risk factors and MoCA total score and subscales was assessed using Pearson’s correlation coefficient (PCC) analysis. It allowed to detect which cognitive domains were affected by every risk factor identified. Finally, repeated-measures-ANOVAs (RM-ANOVA) (between-subject factor “Predisposing factors”, within-subject factors “alpha” and “beta” EEG bands) were performed to detect the effects of risk factors on alpha and beta EEG measurements. Results are expressed as mean (SD) unless otherwise stated. Bonferroni corrected t tests were used for post-hoc analysis ($p < 0.01$).

Results

A preliminary analysis was performed on the MoCA subscales. Repeated-measures-ANOVAs (RM-ANOVA) (between-subject factor “groups”, within-subject factors “subscales”) were performed: 2 (Groups) X 10 (Subscales: visuospatial/executive functions, naming, forward and backward digit span, target detection task, serial subtraction task, repetition of sentences, language fluency, abstraction, memory, orientation).

Table 2 shows the means and standard deviation of MoCA with reference to both global and subscale scores, for each of interested groups, experimental and control. The factor “groups” show significant effects, $F(1, 98) = 5846.39, p < .001$. With reference to the MoCA subscales RM-ANOVA revealed a significant effect of the interaction “Groups X Subscales”, $F(9, 882) = 30.36, p < .001$.

The experimental group showed lower performances than the control group in the following subtests: visuospatial/executive functions, serial subtraction task, language fluency, abstraction and memory.

	Experimental Group	Control Group
Visuospatial/Executive Functions	1.68 (1.41)	4.46 (0.73)
Naming	2.32 (0.82)	3.0 (0.00)
Forward and backward digit span	1.56 (0.54)	1.98 (0.14)
Target detection task	0.72 (0.45)	1.0 (0.00)
Serial subtraction task	1.42 (1.07)	2.92 (0.27)
Repetition of sentences	1.82 (0.44)	1.98 (0.14)
Language fluency	0.54 (0.50)	1.0 (0.00)
Abstraction	1.30 (0.79)	1.94 (0.24)
Memory	1.56 (1.36)	2.60 (1.41)
Orientation	5.40 (0.90)	6.0 (0.00)
MOCA tot.	19.14 (3.51)	27.62 (1.38)

Table 2: Means (and standard deviations) of the MoCA subscales and total score.

To verify the influence of the predisposing factors that affect cognitive decline, the parameter relative to the total MoCA score, each factor of CSHA- Risk Factors Questionnaire was related to each MoCA subscales. Due to high number of factors Bonferroni correction was used ($p < .001$). Table 3 shows significant positive and negative correlations. Years of education of the subject [$r(100) = 0.50, p < .001$], the qualification obtained [$r(100) = 0.35, p < .001$], leisure activities [$r(100) = 0.36, p < .001$] or mental activity such as reading, writing, playing cards, completing crosswords [$r(100) = 0.33, p < .001$] and finally being engaged in regular physical exercise [MOCA: $r(100) = 0.33, p < .001$] positively influenced the MoCA total score. Whereas some physical, psychiatric/

psychological health conditions such as: stomach ulcer [$r(100) = -0.33, p < .001$], stroke [$r(100) = -0.36, p < .001$], epilepsy [$r(100) = -0.30, p < .001$], the presence of paralysis of some kind [$r(100) = -0.24, p < .001$], learning difficulties [$r(100) = -0.58, p < .001$] and depression [$r(100) = -0.36, p < .001$], quantity of cigarettes smoked by the subject every day (less than one parcel, one parcel, more than one parcel) [$r(100) = -0.47, p < .001$] negatively influenced the MoCA total score.

Factors	Positive Correlations	Factors	Negative Correlations
Years of education		Stomach ulcer	
PCC	+ 0,50**	PCC	- 0,33**
Sig. (2-code)	.000	Sig. (2-code)	.001
Qualification obtained		Stroke	
PCC	+ 0,35**	PCC	-0,36**
Sig. (2-code)	.000	Sig. (2-code)	.000
Leisure Activities		Epilepsy	
PCC	+ 0,36**	PCC	-0,30**
Sig. (2-code)	.000	Sig. (2-code)	.002
Mental Activities		Paralysis of some kind	
PCC	+ 0.33**	PCC	-0,24**
Sig. (2-code)	.001	Sig. (2-code)	.016
Physical Exercise		Learning difficulties	
PCC	+ 0.33**	PCC	-0,58**
Sig. (2-code)	.001	Sig. (2-code)	.000
		Depression	
		PCC	-0,36**
		Sig. (2-code)	.000
		Quantity of cigarettes smoked every day	
		PCC	-0,47**
		Sig. (2-code)	.002

Table 3: Significant correlations between predisposing factors and MoCA total score.

To analyze the influence of each predisposing factors on each MoCA subscale Bonferroni corrected Pearson correlation coefficients (PCC) were used (see table 3). Predisposing factors that positively influence “visuospatial/executive functions” subscale are: years of education [$r(100) = 0.54, p < .001$], qualification

obtained [r (100) = 0.39, p < .001], leisure activities [r (100) = 0.43, p < .001] and physical exercise [r (100) = 0.33, p < .001]; while, factors that negatively influence “visuospatial/executive functions” subscale are: different health conditions as stroke [r (100) = - 0.33, p < .001], diabetes [r (100) = - 0.30, p < .001], learning difficulties [r (100) = - 0.54, p < .001], depression [r (100) = -0.32, p < .001] and quantity of cigarettes smoked every day [r (100) = -0.43, p < .001].

Predisposing factors that positively influence “naming” subscale are: years of education [r (100) = 0.35, p < .001], qualification obtained [r (100) = 0.29, p < .001], leisure activities [r (100) = 0.27, p < .001], while those that negatively influence “naming” subscale are: stroke [r (100) = - 0.34, p < .001], learning difficulties [r (100) = - 0.34, p < .001]. A predisposing factor that positively influences “forward and backward digit span” subscale is years of education [r (100) = 0.33, p < .001], while the factors that negatively influence this subscale are heart attack [r (100) = - 0.34, p < .001], stroke [r (100) = - 0.30, p < .001], learning difficulties [r (100) = - 0.26, p < .001] and depression [r (100) = - 0.27, p < .001]. “Target detection task” subscale, instead, is negatively influenced by thyroid disorders [r (100) = - 0.27, p < .001].

Influencing factors that positively affect “serial subtraction task” subscale are: years of education [r (100) = 0.49, p < .001], qualification obtained [r (100) = 0.38, p < .001], leisure activities [r (100) = 0.35, p < .001], mental activities [r (100) = 0.35, p < .001], while factors that negatively influence it are: stomach ulcer [r (100) = -0.28, p < .001], epilepsy [r (100) = - 0.36, p < .001] and learning difficulties [r (100) = -0.41, p < .001]. Predisposing factors that positively influence “language fluency” subscale are years of education [r (100) = 0.39, p < .001] and qualification obtained [r (100) = 0.28, p < .001], while the factors that negatively influence this subscale are: stroke [r (100) = -0.26, p < .001], learning difficulties [r (100) = - 0.43, p < .001], depression [r (100) = - 0.29, p < .001], quantity of cigarettes smoked every day [r (100) = - 0.42, p < .001]. Influencing factors that positively affect “abstraction” subscale are years of education [r (100) = 0.51, p < .001], qualification obtained [r (100) = 0.35, p < .001], mental activities [r (100) = 0.29, p < .001], while the factors that negatively influence it are: stomach ulcer [r (100) = - 0.28, p < .001], epilepsy [r (100) = -0.31, p < .001], learning difficulties [r (100) = -0.45, p < .001], depression [r (100) = -0.32, p < .001], and quantity of cigarettes smoked every day [r (100) = -0.43, p < .001]. Finally, a predisposing factor that positively influences “orientation” subscale is years of education [r (100) = 0.28, p < .001] while the factors that negatively influence it are paralysis of different kind [r (100) = - 0.35, p < .001] and learning difficulties [r (100) = - 0.30, p < .001].

Table 4 shows means and standard deviations relative EEG measures. The independent t- test showed differences between experimental group and control group: both for alpha and beta, respectively, [t (98) = 2.80, p < .02] and [t (98) = 3.43, p < .001]. The experimental group shows significantly lower levels of alpha and beta values than control group.

	Experimental Group	Control group
Alpha	9.58 (0.85)	10.1(0.92)
Beta	18.14 (2.70)	19 (0.81)

Table 4: Means (and standard deviation) of alpha and beta bands measurements.

To understand whether our predisposing factors could relate alpha or beta values in the experimental group PCCs were applied. No significant correlations were found whereas predisposing factors affected neurophysiological measures. The absence of significant correlations may be due to the low range of variation of alpha and beta bands.

Discussions

This research investigated the potential effect of predisposing factors of cognitive decline on neuropsychological and physiological measurements. In line with literature, the results of the present study, first of all, demonstrate how there is actually an influence of lifestyle in the onset of cognitive decline and diverse major neurocognitive disorders. Analysis revealed significant correlations between performance in cognitive functioning and some of the factors of lifestyle, past or current, considered.

In particular, the level of education of the subject, qualification achieved, practicing or having regularly practiced physical, leisure or mental leisure activities in the free time, engaging in regular exercise, excessive smoking or the presence of specific physical, psychological or psychiatric conditions like stomach ulcer, stroke, epilepsy, the presence of paralysis of some kind, learning difficulties and depression were all associated with cognitive decline and have an impact on the MoCA global scores.

The results of the research have shown again, how a low level of education and not having achieved any qualification are predictive factors in the development of cognitive decline as evidenced by the analysis of Barnes and Yaffe [7], in which the risk of dementia in subjects with a low level of education was 59% higher than those with a high level of education. Practicing leisure activities, mental activities such as writing, reading, playing cards, playing an instrument, and even engaging in regular physical activity (regardless of the type of activity or the weekly frequency), positively correlates with total score of neuropsychological test. From a neuroanatomical perspective, it has been detected that

cognitive activities and socially demanding activities can increase the number of synaptic interconnections between nerve cells and reduce the percentage of hippocampal atrophy compared to individuals with lower levels of activity [13,14]. Physical activity, in particular, seems to increase neuronal function and survival as well as non-neuronal components of the brain such as vascularization [18]. Practicing physical activity could have a positive effect by counteracting the onset of cardiovascular or cerebrovascular problems such as heart attacks or strokes. The latter in fact is one of the pathological conditions that, in this research, negatively correlates with the total score on the MoCA test. From analysis of the data, in fact, it is clear that suffering or having suffered from particular diseases or health conditions such as stroke, epilepsy, the presence of paralysis of some kind, learning difficulties and depression is significantly correlated with cognitive decline. Finally, another factor that presents a significant correlation with low performance to cognitive tests seems to be, not so much the variable smoking itself, as the number of cigarettes smoked by the subject every day (more than one package). This could be explained by considering the relationship between cigarette smoking and the incidence of cardio and cerebrovascular diseases [47].

With regard to the influence of each predisposing factor on each MoCA subscale, as observed for the total score of MoCA, also in this case, predisposing factors that positively influence “visuospatial/executive functions” subscale are years of education, qualification obtained, leisure activities and physical exercise; while, factors that negatively influence “visuospatial/executive functions” subscale are different health conditions such as stroke, learning difficulties, depression and quantity of cigarettes smoked every day. A factor that instead is negatively correlated with this subscale but not with the total score is diabetes. Many studies show that impaired performance on a variety of executive tasks has been reported in older adults with diabetes mellitus (DM), in particular, type 2 DM [48,49]. Physiological data appear to reinforce the likelihood of executive dysfunction in older adults with type 2 DM, potentially because of neuroanatomical changes resulting from impaired glycaemic control, vascular disease, and insulin resistance [50].

As regard “naming” subscale, as for the global scale, predisposing factors that positively influence it are years of education, qualification obtained, and leisure activities, while those that negatively influence it are stroke and learning difficulties. Regarding “forward and backward digit span” subscale, a predisposing factor that positively influences is years of education, while the factors that negatively influence this subscale are heart attack, stroke, learning difficulties and depression.

As observed for the total score of MoCA, also for the “serial subtraction task” subscale the predisposing factors that positively influence it are years of education, qualification obtained, leisure

activities, and mental activities, while factors that negatively influence it are stomach ulcer, epilepsy and learning difficulties. A factor that negatively influences “Target detection task” subscale, but not global score of the MoCA test, consists of thyroid disorders. Most studies support a relationship between thyroid state and cognition, particularly slowed information processing speed, reduced efficiency in executive functions, and poor learning [51].

Predisposing factors that positively influence the “language fluency” subscale are years of education and qualification obtained while the factors that negatively influence this subscale are: stroke, learning difficulties, depression and quantity of cigarettes smoked every day. Concerning the “abstraction” subscale, also in this case, as for the global score, influencing factors that positively affect it are years of education, qualification obtained and mental activities while the factors that negatively influence it are stomach ulcer, epilepsy, learning difficulties, depression and quantity of cigarettes smoked every day. Finally, a predisposing factor that positively influences the “orientation” subscale is years of education while the factors that negatively influence it are paralysis of different kinds and learning difficulties.

In line with a number of approaching and cross-sectional studies that have explored relations between EEG and cognitive decline [32-37], as regards physiological measurement, alpha and beta bands EEG measurements, significant differences were recorded between the experimental and control group inasmuch as these measures have been shown to be more efficient in the latter. The experimental group shows significantly lower levels of alpha and beta values than the control group but no significant correlations were found. The absence of significant correlations may be due to the low range of variation of alpha and beta bands.

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