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ORIGINAL STUDY

NEURO-PSYCHOLOGICAL FUNCTIONS IN DRIVERS WITH CHRONIC RESPIRATORY FAILURE SECONDARY TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT

This work aim at investigating selective-cognitive disfunctions in a sample of drivers suffering from chronic respiratory failure secondary to chronic obstructive pulmonary disease (COPD), in order to: 1) verify whether deficits of global cognitive and/or neuropsychological functions were present in drivers suffering from chronic respiratory failure secondary to COPD; 2) determine influence of chronic respiratory failure secondary to COPD on cognitive and neuro-psychological functions; 3) assess a suiting evaluation protocol based on quantifiable, reproducible and verifiable parameters.

The present study is one of the few which had investigated and found selective-cognitive disfunctions in a sample of drivers with chronic respiratory failure secondary to COPD, in order to assess an evaluation protocol based on quantifiable and verifiable parameters.

KEYWORDS*: respiratory functions; verbal memory; short and long term visuo-spatial memory; attention, executive functions; praxis.*

1. Introduction

Chronic Obstructive Pulmonary Disease (i.e. COPD) had many names in the past including: Chronic Obstructive Airways Disease, (COAD); Chronic Obstructive Lung Disease, (COLD); Chronic Airflow Limitation, (CAL or CAFL) and Chronic Airflow Obstruction. COPD actually comprises two related diseases, chronic bronchitis and emphysema, one rarely occurring without a degree of the other.

The definition of COPD, that is recognized by both the American Thoracic Society and the European Respiratory Society, is a disorder that is characterized by reduced maximal expiratory flow and slow forced emptying of the lungs; features that do not change markedly over several months. COPD is characterized by airflow limitation caused by chronic bronchitis or emphysema. Frequently, this limitation in airflow is not reversible or only minimally reversible with bronchodilators. Reversible bronchoconstriction

often plays a role in the cause of COPD, but its true magnitude remains to be determined [1].

COPD can cause impairment of neuro-psychological functions and development of cognitive decline [2-9] and it might, therefore, reduce driving abilities, such as Parkinson's disease, Multiple Sclerosis, Stroke, Dementia etc. do, by weakening in drivers perception, information processing and decision making skills etc., and by impairing visual and visuospatial cognitive and psychomotor functions, as well as attentive resources [10-22].

So this work aim at investigating selective-cognitive disfunctions in a sample of drivers suffering from chronic respiratory failure secondary to COPD, in order to:

- verify whether deficits of global cognitive and/or neuropsychological functions were present in drivers suffering from chronic respiratory failure secondary to COPD,
- determine influence of chronic respiratory failure secondary to COPD on cognitive and neuro-psychological functions,
- assess a suiting evaluation protocol based on quantifiable, reproducible and verifiable parameters.

To achieve such goals we intended to assemble a comprehensive set of both pneumological exams and tests for global cognitive and neuropsychological functions evaluation, even if the examination of cognitive function is not the part of the basic set of tests which is carried out in patients with COPD.

2. Material and methods

Population recruitment

In this study we proceeded to recruit a population of two groups:

1) Group of patients (P), admitted to the hospital for a respiratory rehabilitation program, was compound of 20 licensed drivers (years of possess of driving license more than 20), who used to drive at least twice/week, (10 women and 10 men), aged 50 to 70 years and affected by COPD with chronic respiratory failure. A diagnosis of COPD was made according to the GOLD Guidelines.[23] All patients were in stable clinical conditions, as assessed by an arterial pH of > 7.35, were receiving long-term oxygen therapy and had not experienced an exacerbation of their condition in the preceding 4 weeks. Patients with comordity of psychiatric and neurological diseases determining alteration of cognitive functions and comordity of visual, campimetric and hearing diseases (insufficient perception of simple and compound phonemes at distance of 2 mt) or other pulmonary diseases as Sleep Apnea Syndrome were excluded from the present study.

2) Group of Controls (C): 20 healthy subjects owning a driving license (holding driving license more than 20 years), who used to drive at least twice/week, (10 women and 10 men), aged 50 to 70 years with general good health.

Subjects with psychiatric and neurological diseases causing alteration of cognitive functions, visual, campimetric and hearing diseases (insufficient perception of simple and compound phonemes at distance of 2 mt) and respiratory or cardiovascular diseases were excluded from the study.

Such a recruitment involved the Fondazione "Ospedale S. Raffaele – Giglio", Department of Re-Habilitation - Cefalù (PA) in individuating and requesting participation of suiting subjects (registered from January 2007 to November 2009).

To be eligible for enrollment, participants were required to have a valid driver's license, and to confirm that they all were active drivers during the baseline visit, by affirming to be used to drive twice/week at least.

Such a cohort was not a population-based sample of older drivers, since criteria for inclusion and exclusion – as briefly described afterward - were applied in order to select suitable patients and controls.

Evaluation Procedures

Evaluation of Patients and Controls has considered history and medical status of each subject who underwent the examination. Both has been submitted to:

- pulmonary function tests, indicating the degree of bronchial obstruction, included measurements of FEV1 and forced vital capacity (FVC) before and after 15 minutes from the inhalation of 200 μg of salbutamol. Spirometry was performed according to the American Thoracic Society Guidelines [24]. Flows and volumes were measured with spirometer (6200 Autobox Pulmonary Function Laboratory; Sensormedics, Yorba Linda, CA). The predicted normal values used were those from the European Community for Steel and Coal [25].
- 30 min. diurnal oximetry was sampled by oximeter model: CMS-50C Contec Medical System with patients at rest in a semi-recumbent position. Normal subjects breathing room air, patiences receiving oxygen as prescribed during the evaluation at the admission in the Department of Re-Habilitation.

Only patients have been submitted to:

- Arterial blood gas analysis arterial blood was sampled at the radial artery with patients in a semi-recumbent position and breathing oxygen. Pao2, Paco2, and pH were measured by means of an automated analyzer (model 840; Ciba Corning; Medfield, MA).
- 6 min. Walking test: was performed according to the American Thoracic Society Guidelines [1].

Then we proceeded to the evaluation of their pulmonary functions by administering Spirometry and 30 min. diurnal oximetry.

Only patiences have been submitted to arterial blood gas analysis and 6 min. Walking test.

Neuro-psychological evaluation was carried out by submitting to the individuated groups the following tests in order to appraise their global cognitive functions (by Mini Mental State Examination) and some neurological functions such as short and long term verbal memory, short and long term visuo-spatial memory, attention, executive functions (cognitive flexibility and planning) and praxis.

Particularly, following tests were applied for *assessment of memory*:

- Digit Span Forward: Short Term Verbal Memory
- Rey's Lists IR and DR
- Rey's Figure Recall for both visuo-spatial long term memory and coordination skills
- Semantic Flow Test for long term verbal memory
- Corsi's Test for short term visuo-spatial memory

To assess *executive functions*, instead, were used neuro-psychological tests as these following:

- Digit Span Backward for both long term verbal memory and executive functions
- Phonemic Flow Test for both long term verbal memory and executive functions
- 36 P.M. Raven
- Frontal Assessment Battery (FAB)
- Tower of London for planning abilities and cognitive flexibility

Moreover, neuro-psychological tests were also submitted to both the groups in order to evaluate their *attention*:

- Trail Making Test A
- Trail Making Test B
- Trail Making Test AB

All of the latter were used to appraise visual elaborations, motor speed and shifting abilities (Reitan RM, 1958).

Finally we also checked *praxis* by submitting to patients and controls Neuro-Psychological Tests as:

- Rey's Figure Copy: either visuo-spatial long term memory or coordination skills [26].
- Visual Motor Paxis: coordination skills [27].

Descriptive Statistical Analysis

Data registered with regard to pneumological and neuro-psychological tests were all collected on an excel database, so that differences between groups (Patients Vs Controls) could be evaluated.

Such Data, corrected on the base of subjects' age and number of years of study, were also examined considering possible differences between two sub-populations (Male patients vs. Female patients) in order to highlight their significance, and as means and variances; variances coefficients were calculated.

In order to assess the above comparison and to test for differences among the groups, the one-way analysis of variance (One-way ANOVA) was used to is used: T-test and Fisher's Statistic.

The statistical level of significance was set at $P < 0.005$ (significant); $P < 0.001$ (very significant) $P < 0.0001$ (extremely significant).

3. Results

The Tests carried on a population compound of 20 patients (10 Male + 10 Female) and 20 controls (again 10 Male + 10 Female), recruited on the base of criteria above presented, were focused firstly on a examining **respiratory functionality**, then on valuating **global cognitive functions** and finally on verifying possible **neuro-psychological deficits** correlated to altered parameters. Measures taken are represented in following tables (Tables I –VIII).

Since all of the patients were in LTOT (Long Term Oxygen Therapy), in stable conditions (no re-acerbating of pulmonary diseases since 3 weeks at least), they had 29.01% FiO_2 mean values.

As resulting from data above represented, spirometry showed:

- Forced Vital Capacity (FVC %) – Media value 70.85%
- Forced Expiratory Volume (FEV1 %) - Media value 34.60%
- Relation between Forced Expiratory Volume and Forced Vital Capacity (FEV1/FVC %) - Media value 45.66%

Also results for emo-gas analysis showed:

- Pondus Hidrogenii (PH) - Media value 7.39
- Carbon Dioxide Arterial Pressure (PaCO2 mmHg) - Media value mmHg 45.74
- Arterial Oxigen Pressure (PaO2 mmHg) - Media value mmHg 76.52

Finally, the 6 Minutes Walking Test showed reduced capacity of physical exercises: Media value m. 321.15.

Specific tests on sample have shown deficits in several neuro-psychological functions.

Values registered for Patients and Controls are as following (tables V-VIII):

ANOVA between means variables of Male Patients vs Female Patients did not show any relevant difference as represented in the following graphic (table X, figure 1)

Tests also showed a **Prevalence** of deficits as well exposed in the figure below (figure 2).

The entire sample (100%) showed deficits of executive functions, of planning abilities and problem solving; 94% of sample showed deficits of long-term verbal memory; 69% of sample showed deficits of short-term verbal memory; 56% of sample showed deficits of short-term visuo-spatial memory; 50% of sample showed deficits of long-term visuo-spatial memory.

TableI. *Male Patients (PM)*

STRUMENTAL TEST	PM1	PM2	PM3	PM4	PM5	PM6	PM7	PM8	PM9	PM10
FVC %	114.00	60.00	54.00	88.00	80.00	62.00	75.00	86.00	37.00	73.00
FEV1 %	83.00	35.00	24.00	44.00	33.00	34.00	36.00	42.00	18.00	20.00
FEV1/FVC %	55.00	47.00	44.00	40.00	41.00	55.00	48.00	49.00	39.00	43.00
Walking test	360.00	360.00	300.00	330.00	100.00	400.00	330.00	400.00	300.00	350.00
PH	7.39	7.40	7.41	7.41	7.42	7.35	7.39	7.42	7.36	7.34
PaCO2 mmHg	49.20	40.70	44.40	38.90	36.00	60.80	42.00	37.00	58.30	51.70
PaO2 mmHg	70.50	98.00	84.40	70.10	74.00	76.50	70.00	75.00	68.10	68.60
FiO2	33.00	33.00	28.00	33.00	28.00	33.00	33.00	28.00	33.00	28.00
PaCO2 mmHg RA	43.10	38.90	44.0	37.00	36.00	55.10	40.00	37.00	55.20	47.90
PaO2 mmHg RA	50.30	54.00	52.70	46.20	53.00	48.50	45.00	50.00	47.10	52.60

Table II. *Male Controls (CM)*

STRUMENTAL TEST	CM1	CM2	CM3	CM4	CM5	CM6	CM7	CM8	CM9	CM10
FVC%	85.00	90.00	104.00	87.00	105.00	100.00	95.00	100.00	99.00	110.00
FEV1%	88.00	100.00	99.00	77.00	100.00	95.00	88.00	93.00	88.00	100.00
FEV1/FVC%	83.00	89.00	76.00	71.00	76.20	76.00	74.00	74.00	71.00	72.00

Table III. *Female Patients (PF)*

STRUMENTAL TEST	PF1	PF2	PF3	PF4	PF5	PF6	PF7	PF8	PF9	PF10
FVC %	60.00	88.00	55.00	88.00	80.00	85.00	90.00	70.00	37.00	75.00
FEV1 %	35.00	44.00	26.00	44.00	38.00	35.00	45.00	34.00	18.00	36.00
FEV1/FVC %	47.00	40.00	47.00	40.00	47.00	41.00	50.00	49.00	39.00	48.00
Walking test	360.00	330.00	300.00	330.00	330.00	380.00	360.00	280.00	240.00	280.00
PH	7.39	7.41	7.41	7.40	7.38	7.39	7.36	7.37	7.36	7.39
PaCO2 mmHg	40.70	38.90	44.40	38.90	50.00	39.00	48.00	43.00	58.30	42.00
PaO2 mmHg	68.00	72.00	84.40	65.30	65.00	70..00	67.00	64.00	68.10	70.00
FiO2	33.00	33.00	28.00	28.00	28.00	33.00	28.00	28.00	28.00	33.00
PaCO2 mmHg RA	38.70	37.00	44.80	35.80	46.50	39.00	49.00	40.00	58.00	42.20
PaO2 mmHg RA	48.00	46.20	50.40	46.20	52.00	45.00	53.00	50.00	52.30	45.30

Table IV. *Female Controls (CF)*

STRUMENTAL TEST	CF1	CF2	CF3	CF4	CF5	CF6	CF7	CF8	CF9	CF10
FVC%	100.00	95.00	90.00	99.00	105.00	87.00	95.00	90.00	98.00	95.00
FEV1%	100.00	87.00	95.00	87.00	100.00	90.00	87.00	95.00	90.00	87.00
FEV1/FVC%	100	73.00	84.00	71.00	76.00	82.00	73.00	84.00	73.00	73.00

Table V. *Neuro-psychological tests in Male Patients (PM)*

NEURO-PSYCHOLOGICAL TEST	PM1	PM2	PM3	PM4	PM5	PM6	PM7	PM8	PM9	PM10	CUT OFF
MMSE	29.03	25.29	20.99	26.27	30.01	25.99	27.99	25.99	25.97	20.99	24.00
Digit span Forward	6.00	4.75	2.75	4.50	5.50	3.75	4.75	3.75	6.00	5.25	3.75
Ray's List RI	41.20	24.40	20.40	25.40	36.60	23.40	41.50	23.40	30.20	36.00	28.53
Ray's List RD	7.80	3.20	1.20	7.20	7.20	2.20	9.00	2.20	7.60	6.30	4.69
Semantic Flow	47.00	35.00	0,83	24.00	30.00	25.00	41.00	25.00	35.00	47.00	25.00
Rey's Figure Recall	4.50	15.25	0,00	11.25	11.75	7.25	23.00	7.25	12.25	0,00	9,45
Corsi's Test	7.53	1.00	4.75	3.75	4.25	3.75	5.75	3.75	4.50	5.00	3.50
Digit Span Backward	3.00	2.00	2.00	3.00	5.00	2.00	4.00	2.00	3.00	1.00	5-9
36 p.m. Raven	23.00	20.50	30.00	31.50	26.50	25.50	32.50	25.50	26.50	30.00	17.50
Fonemic Flow	23.00	16.00	0,00	26.00	25.00	20.00	23.00	20.00	31.00	29.00	17.35
FAB	12.53	16.59	11.97	8.97	15.81	12.43	14.43	12.43	17.00	16.80	12.03
Tower of London	12.00	18.00	29.00	10.00	9.00	20.00	16.00	20.00	19.00	27.00	27.00
TMT-A (sec.)	241.00	130.00	219.00	199.00	130.00	150.00	75.00	150.00	68.00	44.00	94.00
TMT-B (sec.)	378.00	159.00	340.00	358.00	208.00	188.00	158.00	188.00	121.00	62.00	283.00
TMT A-B (sec.)	699.00	39.00	160.00	159.00	79.00	163.00	83.00	163.00	53.00	18.00	187.00
Rey's Figure Copy	36.00	36.00	36.00	27.50	36.00	36.00	34.50	36.00	36.00	35.50	30.04
Ideo-motor Praxis	18.50	19.75	19.75	19.75	20.25	19.75	20.00	19.75	19.75	19.75	16.00

Table VI. *Neuro-psychological tests in Male Controls*

NEURO-PSYCHOLOGICAL TEST	CM1	CM2	CM3	CM4	CM5	CM6	CM7	CM8	CM9	CM10	CUT OFF
MMSE	27.99	29.54	28.53	28.46	29.53	27.03	28.03	26.53	2746	28.03	24.00
Digit span Forward	4.75	6.50	5.75	6.25	4.75	5.50	5.75	5.50	5.25	5.75	3.75
Ray's List RI	41.50	51.50	48.00	36.60	31.30	34.00	38.30	35.50	36.50	36.60	28.53
Ray's List RD	9.0	11.90	9.30	6.20	8.60	7.30	13.20	8.10	9.10	6.20	4.69
Semantic Flow	41.00	46.00	36.00	47.00	39.00	29.00	33.00	45.00	48.00	47.00	25.00
Rey's Figure Recall	23.00	29.00	24.50	25.50	26.50	30.25	21.50	24.00	25.25	25.50	9.45
Corsi's Test	5.75	6.00	6.75	5.00	6.25	4.25	5.75	4.00	5.50	5.00	3.50
Digit Span Backward	4.00	5.00	3.00	5.00	5.00	4.00	5.00	4.00	5.00	4.00	5-9
36 p.m. Raven	32.50	33.00	35.50	34.50	35.50	36.00	33.50	35.50	35.00	36.00	17.50
Fonemic Flow	23.00	34.00	21.00	33.00	27.00	38.00	35.00	28.00	32.00	38.00	17.35
FAB	14.43	17.43	15.81	18.01	16.01	15.00	17.01	16.43	17.43	15.00	12.03
Tower of London	36.00	29.00	30.00	34.00	33.0	28.00	32.00	27.00	27.00	28.00	27.00
TMT-A (sec.)	55.00	44.00	60.00	66.00	90.00	70.00	80.00	67.00	60.00	55.00	94.00
TMT-B (sec.)	76.00	50.00	75.00	70.00	85.00	75.00	87.00	77.00	75.00	76.00	283.00
TMT A-B (sec.)	25.00	18.00	53.00	46.00	93.00	67.00	95.00	75.00	53.00	25.00	187.00
Rey's Figure Copy	36.00	35.00	34.50	35.00	36.00	36.00	36.00	35.00	34.00	36.00	30.04
Ideo-motor Praxis	19.75	19.75	20.00	19.25	20.00	20.25	20.00	19.25	20.00	19.75	16.00

Table VII. *Neuro-psychological tests in Female Patients*

(PF)

NEURO-PSYCHOLOGICAL TEST	PF1	PF2	PF3	PF4	PF5	PF6	PF7	PF8	PF9	PF10	CUT OFF
MMSE	25.29	26.27	23.97	25.99	27.99	25.29	20.99	26.27	25.97	29.74	24.00
Digit span Forward	4.75	4.50	2.75	3.75	4.75	4.75	2.75	4.50	6.00	5.50	3.75
Ray's List RI	24.40	25.40	23.40	23.40	41.50	24.40	20.40	25.40	30.20	27.80	28.53
Ray's List RD	3.20	7.20	3.20	2.20	9.00	3.20	1.20	7.20	7.60	7.20	4.69
Semantic Flow	35.00	24.00	20.00	25.00	41.00	35.00	20.00	24.00	35.00	24.00	25.00
Rey's Figure Recall	15.25	11.25	8.25	7.25	23.00	15.25	2.25	11.25	12.25	11.25	9.45
Corsi's Test	1.00	3.75	4.75	3.75	5.75	1.00	4.75	3.75	4.50	3.75	3.50
Digit Span Backward	2.00	3.00	2.00	2.00	4.00	2.00	2.00	3.00	3.00	3.00	5-9
36 p.m. Raven	20.50	31.50	30.00	25.50	32.50	20.50	30.00	31.50	26.50	31.50	17.50
Fonemic Flow	16.00	26.00	18.00	20.00	23.00	16.00	15.00	26.00	31.00	26.00	17.35
FAB	16.59	8.97	11.97	12.43	14.43	16.59	11.00	8.97	17.00	8.97	12.03
Tower of London	18.00	10.00	19.00	20.00	16.00	18.00	29.00	10.00	10.00	10.00	27.00
TMT-A (sec.)	130.00	199.00	219.00	150.00	75.00	130.00	219.00	199.00	68.00	199.00	94.00
TMT-B (sec.)	159.00	358.00	340.00	188.00	158.00	159.00	340.00	358.00	121.00	358.00	283.00
TMT A-B (sec.)	39.00	159.00	160.00	163.00	83.00	39.00	160.00	159.00	53.00	159.00	187.00
Rey's Figure Copy	36.00	27.50	36.00	27.50	35.75	14.75	35.75	28.75	36.00	27.50	30.04
Ideo-motor Praxis	19.75	19.75	19.75	19.75	19.75	20.00	19.75	20.00	19.75	19.75	16.00

Table VIII. *Neuro-psychological tests in Female Controls (CF)*

NEURO-PSYCHOLOGICAL TEST	CF1	CF2	CF3	CF4	CF5	CF6	CF7	CF8	CF9	CF10	CUT OFF
MMSE	27.99	29.29	28.03	25.46	28.53	29.53	27.53	29.29	28.53	28.03	24.00
Digit span Forward	5.75	4.75	0.75	4.50	5.25	6.50	5.25	4.75	5.25	0.75	3.75
Ray's List RI	44.30	49.30	68.00	44.50	49.25	46.10	49.25	49.30	49.25	68.00	28.53
Ray's List RD	9.00	7.00	14.50	9.10	11.10	10.80	11.10	7.00	9.00	14.50	4.69
Semantic Flow	41.00	47.00	40.00	30.00	45.00	30.00	45.00	47.00	41.00	40.00	25.00
Rey's Figure Recall	23.00	25.50	27.75	26.59	26.50	27.50	26.50	25.50	23.00	27.75	9.45
Corsi's Test	5.25	8.50	5.00	4.25	6.25	5.25	6.25	8.50	5.25	5.00	3.50
Digit Span Backward	4.00	4.00	3.00	5.00	5.00	4.00	5.00	4.00	5.00	6.00	5-9
36 p.m. Raven	32.50	30.50	26.00	27.50	31.00	28.50	30.50	26.00	30.50	32.50	17.50
Fonemic Flow	23.00	33.00	27.00	13.00	29.00	30.00	33.00	27.00	33.00	23.00	17.35
FAB	14.43	17.01	18.43	17.01	18.34	14.34	17.01	18.43	17.01	14.43	12.03
Tower of London	16.00	28.00	33.00	31.00	25.00	30.00	28.00	33.00	28.00	16.00	27.00
TMT-A (sec.)	75.00	44.00	54.00	75.00	56.00	40.00	47.00	66.00	56.00	56.00	94.00
TMT-B (sec.)	158.00	54.00	75.00	90.00	79.00	50.00	59.00	70.00	79.00	79.00	283.00
TMT A-B (sec.)	83.00	14.00	20.00	95.00	27.00	65.00	70.00	75.00	27.00	27.00	187.00
Rey's Figure Copy	36.00	35.75	14.75	35.75	28.75	34.50	35.75	14.75	28.75	36.00	30.04
Ideo-motor Praxis	19.75	20.00	19.75	20.00	20.00	20.00	20.00	19.75	20.00	20.00	16.00

Such measurements have shown Statistic Significance for Patients vs Controls. Particularly Anova method showed relevant differences between the groups (< 0.05%) except for Rey’s figure copy and visuo-spatial praxia (Table 9).

Table IX. *One Way Analysis of Variance*

NEURO-PSYCHOLOGICAL TEST	*F*	*F crit*	*P*
MMSE	13.919	4.196	< .001
Digit span Forward	5.897		< .05
Ray's List RI	37.520		< .001
Ray's List RD	27.318		< .001
Semantic Flow	20.637		< .001
Rey's Figure Recall	61.123		< .001
Corsi's Test	15.692		< .001
Digit Span Backward	28.226		< .001
36 p.m. Raven	8.008		< .01
Fonemic Flow	15.402		< .001
FAB	22.675		< .001
Tower of London	27.163		< .001
TMT-A (sec.)	53.260		< .001
TMT-B (sec.)	47.567		< .001
TMT A-B (sec.)	15.368		< .001
Rey's Figure Copy	0.0002		> .5
Ideo-motor Praxis	0.041		> .5

Origin of Variance: Between Groups (Patients+Controls) P>=0.05

Table X. *Fisher’s Two-Tailed Z Test*

NEURO-PSYCHOLOGICAL TEST	MEANS		Z	TWO-TAILED Z TEST
	PM	PF		
MMSE	26.445	24.885	1.960	1.256
Digit span Forward	4.469	4.063		0.905
Ray's List RI	29.538	25.663		1.066
Ray's List RD	5.000	4.300		1.488
Semantic Flow	30.875	28.000		0.710
Rey's Figure Recall	10.031	10.406		-0.107
Corsi's Test	4.316	3.563		0.895
Digit Span Backward	2.875	2.500		0.836
36 p.m. Raven	26.875	27.750		-0.409
Fonemic Flow	19.125	15.875		0.731
FAB	13.145	12.740		0.319
Tower of London	16.750	18.750		-0.616
TMT-A (sec.)	161.75	165.125		-0.136
TMT-B (sec.)	247.125	257.500		-0.230
TMT A-B (sec.)	193.125	120.250		1.013
Rey's Figure Copy	34.75	30.250		1.704
Ideo-motor Praxis	19.688	19.813		-0.718

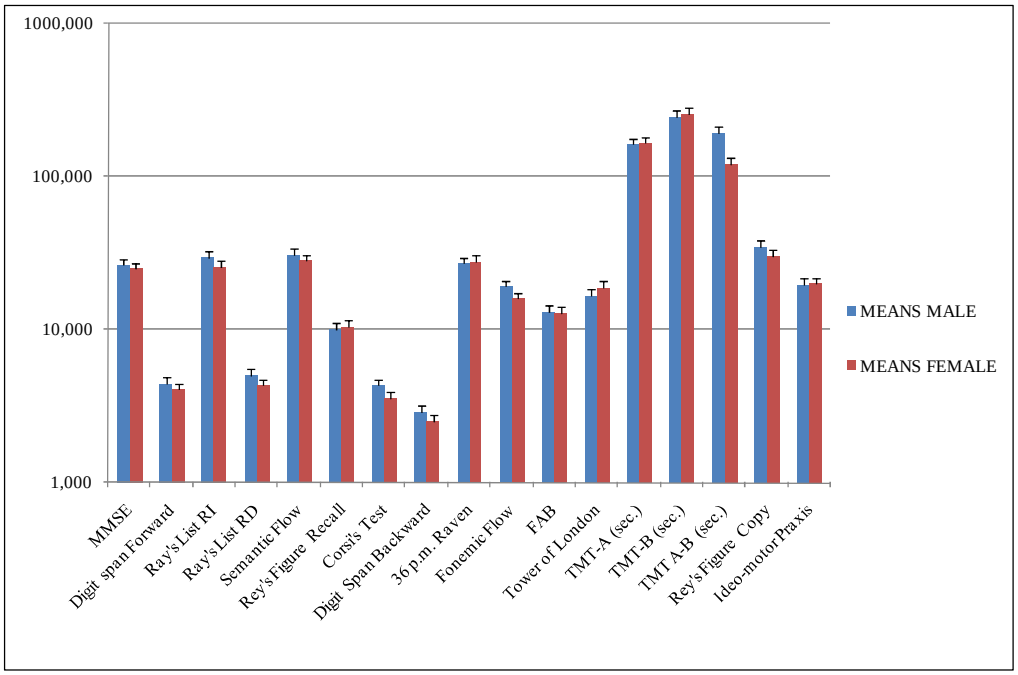

Figure 1. *Statistic Significance Male Patients vs Female Patients*

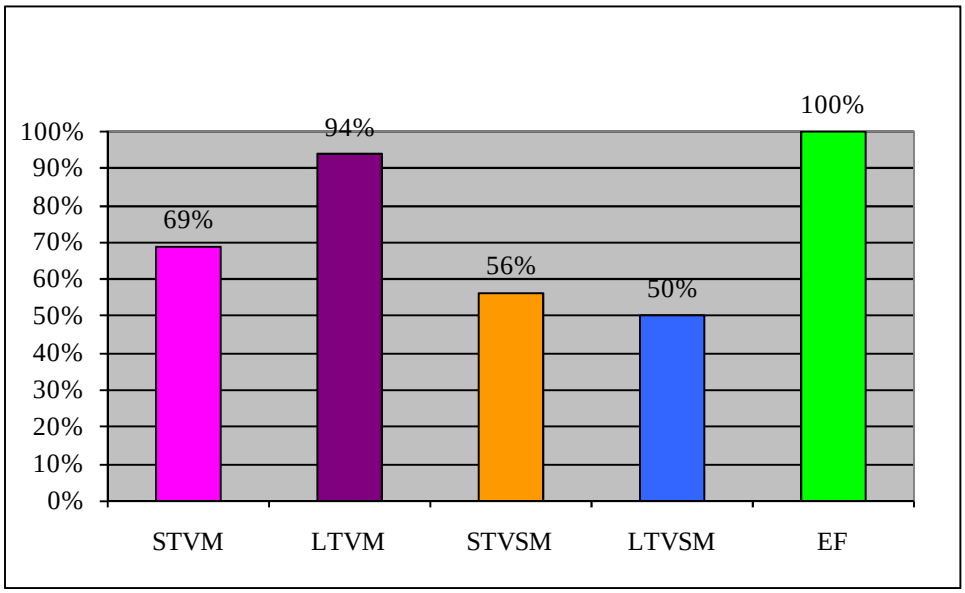

Figure 2. *Prevalence of deficits.*
STVM: short-term verbal memory; LTVM: long-term verbal memory; STVSM: short-term visuo-spatial memory; LTVSM: long-term visuo-spatial memory; EF: executive functions

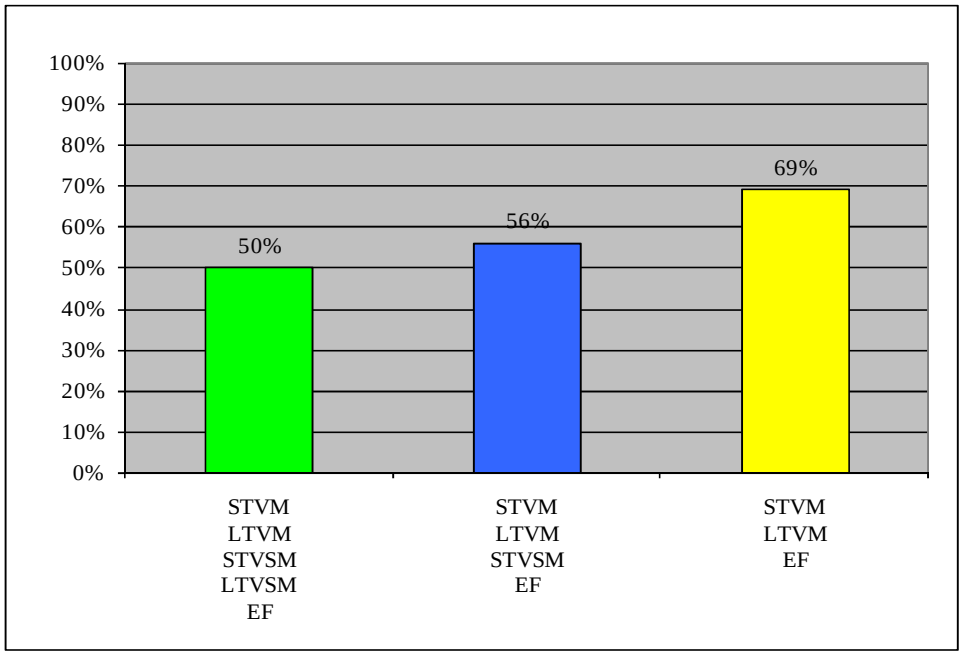

Figure 3. *Coexistence of deficits*
STVM: short-term verbal memory; LTVM: long-term verbal memory; STVSM: short-term visuo-spatial memory; LTVSM: long-term visuo-spatial memory; EF: executive function

Finally the following histogram shows **coexistence** of deficits, since 50% of sample had altered all of the functions (executive functions, the short term visuo-spatial memory, short term verbal memory and executive functions), 56% of sample showed an alteration of the following functions (executive functions, short term verbal memory , long term verbal memory and the short term visuo-spatial memory), 69% of sample had altered executive functions and both short and long term verbal memory (figure 3).

4. Discussions

Car driving is a situation in which several attentional aspects (e.g., simple and selective attention and vigilance) are engaged. It is a highly complicated form of activity carried out in a constantly changing environment. It consists of perception, information processing, and decision making and requires the drivers to carry out simultaneous tasks (steering, braking, and accelerating) which in particular stress the visual and visuospatial cognitive and psychomotor functions, as well as attentive resources [16,18,21,22]

So different attentional aspects are crucial to car driving performance: simple attention is relevant in terms of breaking reactions, divided attention resembles driving in a city with much traffic, and vigilance is engaged when the driving situation is long-term under monotonous conditions.Visuospatial difficulties, neglect, reduced psychomotor speed, and executive dysfunctions, are listed as impairments contrary to safe driving, as well as slowed reaction time, impaired visuoconstructive abilities, and reduced visual scanning are reported as the more prominent impediments to safe driving.

Even if the examination of cognitive function is not the part of the basic set of tests which is carried out in patients with COPD, however there are some theoretical reports and sparse publications indicating the impairment of these functions among patients with COPD: some study had suggested an association between COPD and the development of cognitive decline, some other relates such neurological abnormalities to the degree of hypoxemia, but even non-hypoxemic patients with COPD have shown significant impairments in cognitive performance [28].

Thus COPD can cause impairment of neuro-psychological functions and development of cognitive decline [3-12, 29,30]. Although it is still almost unknown at which extent cognitive deficits can influence driving abilities in patients with COPD (no information about accident frequency in patients with

COPD is yet available); even if no straight correlation seems to exist between the severity of disease, assessed from the polysomnographical findings (e.g., lung function, blood gas analysis, sleep disturbance, nocturnal ventilation, and oxygen saturation), and driving performances [26]; addictionally, despite the fact that not many studies have so far examined drivers with chronic respiratory failure secondary to COPD and their actual abilities for driving, nevertheless, some of the functions essential to driving a car, as the short term working memory, non-verbal recognitive memory, the executive functions and problem solving skills, are often impaired in patients with COPD, who demonstrate significantly worse results in terms of accident frequency in the simulated driving situation as well [29]

Results of the present study confirm that active drivers affected by chronic respiratory failure secondary to COPD show alterations of neuropsychological functions, especially of executive functions, planning abilities and of problem solving (100% of the sample), of short

and long term verbal memory, of short and long term visuo-spatial memory (50% of the sample at least).

Moreover, with regard to attention, even when patients present tests resulting in normal range, we register an increase in reaction-time respect to controls (ANOVA test < 0.01) which is probably supportive for the assumption of deficits, not of attention itself, but of executive functions.

Rey's Figure Copy and Visuo-Spatial Praxia tests did not reveal either relevant discrepancies between Patients and Controls, or significant gender related differences, between men and women.

Yet our results highlight a relation between chronic respiratory failure secondary to COPD and neuro-psychological deficits reducing planning abilities, visuo-spatial and verbal memory (both long and short term) and so making difficult decisions and variations of initial plans.

Therefore, we are inclined to assume that neuro-psychological disfunctions above outlined, may rather be responsible for alterated driving abilities and bad driving simulation performances of patients with COPD.

It coud had been useful to validate our results by an on-road test; but ufortunately, we could not test driving performances of patients showing alterations of executive functions, planning abilities problem solving skills, and memory, in the simulated situation. This is probably the weak point of the present report.

Conversely the strength of this study is the comprehensive set of both pneumological exams and tests for global cognitive and neuropsychological functions, administred in order to verify whether deficits of global cognitive and/or neuropsychological functions were present in drivers suffering from COPD.

In conclusion, despite of limitantions mentioned, which avoided to correlate cognitive disfunctions with driving performances, yet the present study is one of the few which had investigated and found selective-cognitive disfunctions in a sample of drivers with chronic respiratory failure secondary to COPD, in order to assess an evaluation protocol based on quantifiable and verifiable parameters.

5. Conclusions

In fact, since there are no legal indication about how to deal with COPD-patients regarding their driving licensing, while European recommendations concerning the ability to drive a car consider disturbances of gas exchange (e.g., global respiratory insufficiency) or syncope due to coughing as possible risk factors for impaired driving abilities, the results of our study suggest the necessity to assess a protocol capable to better evaluate Executive Functions and Visual and Verbal Memory, and to administrate it to subjects affected by COPD, before releasing or confirming their driving licenses. To achieve significant data, we have found particularly useful the following tests:

Tower of London; Digit Span (Backward & Forward); Rey's List (RI & RD); Corsi's Test.

But we also recommend to add to the protocol a driving test (on road or simulated) for those people affected by COPD whose tests would have resulted in impaired neuro-psychological functions.

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