

Cognitive Reserve and Obstructive Sleep Apnea: The Role of Working Activity in Discriminating Patients from Healthy Controls

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Abstract

Objective: Obstructive sleep apnea (OSA) is a sleep breathing disorder associated with cognitive, social and occupational consequences negatively influencing work performance. This study investigates whether Cognitive Reserve (CR) Working activity and cognitive functioning can discriminate between OSA and healthy participants.

Methods: Sixty-three participants were enrolled and evaluated with the MoCA test and the Cognitive Reserve Index questionnaire.

Results: A logistic regression model highlighted that the CR Working activity ($p < .05$) and the MoCA scores ($p < .01$) predict participants' belonging to GROUP. A Mann-Whitney test did not find differences between patients with High and low CR at the cognitive performance.

Conclusions: Results suggest that CR Working activity and cognitive functioning can discriminate OSA from healthy individuals. However, a difference between OSA patients with high CR and low CR was not confirmed, discouraging the hypothesis of its protective effect in OSA.

Keywords: Obstructive Sleep Apnea Syndrome; Cognitive Reserve; Cognitive Functioning; Working Activity; Occupational Problems

Introduction

The adverse effects of sleep breathing disorders are not just limited to nighttime. It is in fact established that sleepiness and fragmentation of sleep occurring with these diseases can even threaten the individual's overall diurnal well-being [1]. Obstructive sleep apnea (OSA) is the most common sleep breathing disorder [2], and an increasing number of studies is being published about the manifold cognitive, social and occupational consequences associated to it [3]. Although patients are commonly unaware of the nighttime symptoms of OSA, they rather heavily complain about daytime sleepiness, marital problems, and mood disorders [1], which in turn negatively influence work performance. Concentration problems, difficulties in learning new tasks and in carrying-out monotonous ones have been described in OSA patients in their occupational environments [4]. Further

consequences of sleep disorders on workplaces are mortality, accidents and errors, absenteeism, decrease in productivity, and deterioration of interpersonal and professional relationships [5,6]. Interestingly, Sjösten, et al. [7] confirmed that OSA is associated with a risk of work difficulties during approximately six years after the OSA diagnosis, followed by an increased request of disability pensions. Additionally, OSA patients seem to benefit from health care services since even ten years before the actual diagnosis [8], aggravating the socio-economical burden of the syndrome itself. According to some authors [3] the difficulties described on workplaces are consequent to the cognitive impairments associated with OSA. In particular, OSA patients show difficulties in shifting between tasks, in updating and monitoring memory representations, in inhibiting dominant or automatic responses, in generating new information without external input and in fluid

reasoning or problem solving [9]. Such abilities are fundamental for daily life and for work performance: as a matter of facts, impairments in these domains can convincingly be considered an important risk factor for occupational difficulties. As previously mentioned, it has been found that OSA patients benefit from health care services up to 10 years before the diagnosis [8]. This result leads to hypothesize that during this decade, people with OSA may already had experienced difficulties on workplace, and that all that concerns their occupational choices might be negatively influenced by this chronic disease. It is also reasonable to hypothesize that during those approximately ten years before the OSA diagnosis, people may start suffering from cognitive difficulties that contribute exacerbating their overall well-being.

The concept of Cognitive Reserve (CR) refers to the “ability to optimize and maximize performance through the recruitment of brain networks, and/or compensation by alternative cognitive strategies” [10]. It can be estimated by few proxies, of which “Study”, “Education”, “Occupation”, “Intelligence”, and “Leisure Time” are the most recognized [10]. By means of the “Cognitive Reserve Index questionnaire” (CRIq) [10], we aimed to investigate whether the CR related to working activity and the cognitive functioning can predict the participants’ belonging to OSA group. We hypothesized that the measures used can reflect the occupational and cognitive difficulties experienced by OSA patients.

Materials and Methods

A total of sixty-three participants was enrolled for this study: thirty-three patients newly diagnosed with OSA (OSA, mean age 60.37 ± 14.04) and thirty healthy controls (HC, mean age 60.02 ± 12.5). In accordance with the International Classification of Sleep Disorders (2014), inclusion criteria were: a clinical OSA profile and the subjective report of symptoms, and an apnea-hypopnea index (AHI) > 15/h. Exclusion criteria were: Continuous Positive Airway Pressure (CPAP) treatment already ongoing, use of drugs acting on the central nervous system (e.g. benzodiazepines), current or planned intervention for weight reduction, hypertension, diabetes, and other neurological or psychiatric disorders. All these clinical information were collected by expert pulmonologists during the first assessment. The OSA diagnosis was made by means of a portable four-channel device composed of a nasal flow detector, an oximeter, a chest and an abdominal belt able to detect the muscle activity of these regions and the respiratory efforts. Our sample

was made up of patients with a severe level of disease (Mean apnea per hour: 39.5 ± 17.79).

Both groups were matched for age and education. Table 1 shows the descriptive statistics of participants. This study was approved by the local ethic committee and all participants gave their written informed consent to be interviewed and tested.

	Healthy Participants M ± SD	OSAS Patients M ± SD	p-value*
Demographical Characteristics			
Age	60.02 ± 12.5	60.37 ± 14.04	.91
Education	10.02 ± 3.65	9.18 ± 3.58	.36
Neuropsychological Measures			
CRI Total Score	99.58 ± 13.86	95.44 ± 12.54	.22
CRI Education	96.94 ± 12.43	93.37 ± 11.98	.25
CRI Working Activity	101.83 ± 14.02	93.22 ± 7.31	<.05
CRI Leisure Time	100.11 ± 18.63	103.18 ± 15.08	.48
MoCA Test	26.27 ± 2.46	22.59 ± 5.13	<.01

Table 1: Participants’ descriptive statistics. CRI= Cognitive Reserve Index Questionnaire; MoCA Test= Montreal Cognitive Assessment Test; p-value*= U-Mann-Whitney Test; M= Mean; SD= Standard Deviation.

All participants underwent a neuropsychological evaluation including a paper-and-pencil cognitive functioning measure (MoCA, Montreal Cognitive Assessment test), and the CRIq. These measures are shortly described below:

- The MoCA test [11] evaluates the global neuropsychological functioning through items assessing visuospatial abilities, executive functions, short-term memory recall, language and orientation to time and place. According to Santangelo, et al. Italian normative data [12], the cut-off point for the total MoCA score was 15.5/30.
- The CRIq [10] is a standardized instrument aiming to measure the amount of CR that individuals can accumulate during their lifetimes. It includes some demographic data and 20 items grouped into three sections: The CRI-Education

represents the years of total education and possible training courses (lasting at least six months). The raw score of this section is the sum of these two values;

The CRI-Working Activity represents the adulthood professions. Working activities are divided into five levels, according to the degree of intellectual involvement and personal responsibility. The first level is represented by unskilled and manual works (e.g., farmer, car driver, call center operator); the second level regards skilled manual work (e.g., craftsman, clerk, hairdresser). Skilled non-manual or technical works (e.g., trader, kindergarten teacher, real estate agent) represent the third level of working activities, while professional occupation are at the fourth one (e.g., lawyer, psychologist, physician). Highly intellectual occupations represent the highest occupational level (e.g., university professor, judge, top manager). Working activity is recorded as the number of years in each profession over the lifespan. The raw score of this section is the result of years of working activity multiplied by the cognitive level of job (from one to five).

The CRI-Leisure Time represents the cognitively stimulating occupations carried out during leisure time. Sixteen items are related to different intellectual activities (e.g., reading newspaper or books, playing music), social activities (participation in charitable activities, going to museums, travelling), and physical activities (sports, dancing). The frequency (i.e., never/rare, often/always) and the number of years (how long each activity had been carried out) are recorded. The raw score of this section is the total number of years of activity for which frequency is often/always.

Finally, a total CRIq score is provided. It represents the average of the three sub-scores, standardized and transposed to a scale with M = 100 and SD = 15. The CRI can be so classified into five ordered levels: Low (less than 70), Medium-low (70-84), Medium (85-114), Medium-high (115-130) and High (more than 130).

Statistical analyses

A logistic regression model was chosen in order to investigate the role of cognitive reserve and cognitive functioning as predictors of the participants' belonging to GROUP.

In the same model, the total CRI score (CR TOTAL), the CRI score related to education (CR EDUCATION), the CRI score related to working activity (CR WORKING ACTIVITY), the CRI score related

to leisure time (CR LEISURE TIME), and the MoCA test have been considered as main predictors. The GROUP (OSA patients vs. healthy controls) was considered as dependent variable. The model was adjusted for AGE and EDUCATION because of their potential confounding effects on the dependent variable. Collinearity across predictors was checked in the logistic regression model by means of variance inflation factors (VIF) that were found to be lower than 10, thus suggesting no potentially harmful collinearity [13,14] (Bowermann and O'Connel, 1990; Myers, 1990).

A Mann-Whitney test was then conducted in order to compare MoCA performance of OSA patients with High CR (n = 11) with those with low CR (n = 22). According to Nucci., et al. [10] High CR is defined as a TOTAL CRI ≥114, while Low CRI is defined as a TOTAL CRI <114. A two-sided P < 0.05 was considered for statistical significance. Data were analyzed with SAS software, version 9.4 (SAS Institute Inc, Cary, NC).

Results

All CR proxies and the MoCA test scores were analyzed as predictors of GROUP. The logistic regression model highlighted that the CR WORKING ACTIVITY scores (p = .04) and the MoCA scores (p = .001) predict the participants' belonging to GROUP. No significant effects were observed as for the TOTAL CRI (p = .62), the CR EDUCATION (p = .67), and CR LEISURE TIME (p = .58). Table 2 shows complete regression's results.

The Mann-Whitney test did not show any significant difference between OSA patients with High CR and Low CR at the cognitive performance (p = .44).

Model	Standardized Coefficients		
	B (SE)	t	sign.
Age	-.22 (.005)	-1.69	.09
Education	.033	.25	.80
MoCA	-.45 (.01)	-3.53	.001
CRI Total	-2.08 (.15)	-.49	.62
CRI Education	.73 (.07)	.42	.67
CRI Working Activity	-.25 (.005)	-2.04	.045
CRI Leisure Time	1.31 (.06)	-.55	.58

Model	Total sum of squares	df	Average squared	F	sign.
Regression	4.32	4	1.08	5.64	.001
Residue	11.1	58	.19		
Total	15.42	62			

Table 2: Linear regression model.

Dependent variable: GROUP.

Predictors: (constant), Age, Education, MoCA, CRI Total score, CRI Education, CRI Working Activity, CRI Leisure Time.

Discussion

An increasing number of studies is being published about the social, economic and occupational consequences of the Obstructive Sleep Apnea Syndrome. There is evidence that absence from work, frequency of accidents, productivity, progression in career and professional reward are all worse in poor sleepers [15]. Similarly, co-morbidities, self-reported poor efficiency at work and claims for earlier retirement because of acquired disability are more frequent in poor sleepers [16,17]. According to some authors, these problems can be a consequence of a “cognitive frailty” able to aggravate the overall individuals’ well-being [3]. In the present study, we so hypothesized that the Cognitive Reserve (CR) related to working activity and the global cognitive functioning can predict the participants’ belonging to group. Interestingly, results showed that, among all the CR proxies, only the WORKING ACTIVITY one can predict the belonging to GROUP (OSA vs Healthy Controls). Similarly, the MoCA test’s performance was found to distinguish between individuals belonging to the experimental or the control group. On the one hand, people with OSA seem to suffer since a long time before the diagnosis from occupational and work difficulties. This would plausibly decrease their CR related to working activity. So that, OSA patients not just experience problems on their work environments, but they are probably influenced years before the diagnosis in their job and occupational choices. On the other hand, the MoCA test has been found to discriminate between OSA patients and Healthy Controls, highlighting that OSA patients suffer from a “cognitive frailty” that may, in turn, negatively influence their work efficacy and their overall quality of life.

Furthermore, we decided to compare the cognitive performances of OSA patients with High (≥ 114) CR with those with

low (< 114) CR, with the aim to exclude that the results suggested by the previous analyses were just motivated by different levels of cognitive reserve. Surprisingly, there were no difference between OSA patients with High CR and those with low CR at the MoCA test. We so speculated that CR does not protect the brain and a healthy cognitive functioning from the hypoxic damage caused by the syndrome itself. As a matter of facts, we were expecting to find significantly higher scores at the MoCA test in OSA patients with a higher CR compared to those with lower CR. Though, OSA patients seem to not benefit from the protective effects that CR was found to have on other syndromes [18,19].

To the best of our knowledge, Alchanatis., et al. [20] has been the first author who tried to study CR in OSA patients. Because of a lack of measure of CR, the authors chose to investigate this concept through the evaluation of general intelligence (measured with the Raven Matrices, [21]). Alchanatis., et al. [20] found that OSA patients with normal intelligence showed some cognitive deficits (i.e. longer reaction time, attentional deficits), compared to healthy controls matched for age and intelligence. Conversely, OSA patients with high-intelligence showed no cognitive impairments at all, compared to high-intelligence controls. Alchanatis., et al. [20] so suggested that such results were due to the protective effects of the high premorbid functioning level. Although these results are extremely interesting and fascinating, we would tend to discourage the Alchanatis., et al. ones. As a matter of facts, although intelligence has been previously used as proxy of CR, nowadays new and more appropriate measures are available in measuring CR. We draw our conclusions by means of a standardize and currently well recognized measure to quantify the amount of CR, such as the CRIq. In addition, it is significant that the CR related to Working activity was the only proxy able to discriminated the participants’ belonging to group. Nor the TOTAL, the EDUCATION or LEISURE-TIME CRI were found to be predictors of the group belonging, although for some of them (i.e. TOTAL score and EDUCATION CRI), an effect was expected. It is so possible that the difficulties experienced by OSA patients are able to influence their social and occupational experiences, undermining their global quality of life. Routine occupational medicine examinations should include practical and feasible tools to early identification of OSA [22].

Limitations

This study has certainly some weaknesses that have to be acknowledged. First of all, in the cohort of newly diagnosed OSA

patients, the AHI was defined to be > 15 (as suggested by the literature). However, it is also well recognized that a difference between moderate (AHI between 15-29) and severe (AHI > 30) OSA exists and determines different cognitive impairments. Because of the small sample size, in this study it was not possible to differentiate two cohorts of patients according to OSA severity. Furthermore, it is well known that patients with OSA also have a number of comorbidities: another limitation of this study is that we were not able to control for them, as well as data about BMI is lacking.

Conclusions

The present study showed that, among all the CR proxies, only the CR WORKING ACTIVITY can predict the belonging to GROUP. Individuals' performance at the MoCA test was also found to distinguish between those belonging to the experimental or to the control group. It could be so proposed that the CR related to Working activity and the global cognitive functioning are able to properly discriminate individuals with OSA from healthy ones. However, a difference between OSA patients with high CR and those with low CR was not confirmed, leading us to discourage the hypothesis of a protective role of CR in this chronic disease.

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