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Original Article

Exercise training influence on cognitive capacity and mental health within chronic obstructive pulmonary disease – A pilot study

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Abstract

Objective: Although pulmonary rehabilitation and regular exercise have improved negative emotions and cognitive capacity within cases of chronic obstructive pulmonary disease (COPD), influence by exercise training upon different cognitive and memory functions in COPD is still controversial. This investigation aimed to assess whether cognitive performance and mental health are affected by the benefits of exercise training within cases of COPD. **Materials and Methods:** This pilot investigation included thirty-three patients with Global Initiative for Chronic Obstructive Lung Disease stage ≥B. Based on the subjects' rights, all included patients could choose to join either the exercise group or the control group, according to their free will. Twelve patients were assigned to receive exercise treatment over a 2-month period, while the remaining 16 patients were assigned to the control group. Cognitive capacity outcomes were measured using the Wechsler Memory Scale-III Word List Test, Stroop task, and psychomotor vigilance task (PVT). Mood states were assessed through the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI). **Results:** Most cases demonstrated major improvement for BDI and BAI scorings post-60-day therapy. During PVT, the omission rate decreased, while the hit rate increased, indicating an improvement in attention performance. Furthermore, this investigation found a significant increase in immediate verbal and recognition memory for word–list test. However, no major performance shifts were found on Stroop analysis. **Conclusion:** This investigation demonstrated that a 2-month exercise training program resulted in significant improvement in negative emotions, immediate memory, recognition memory, and attention.

Keywords: *Chronic obstructive pulmonary disease, Cognitive capacity, Mental health, Pulmonary rehabilitation*

Introduction

Chronic obstructive pulmonary disease (COPD) reflects an irreversible airflow-restricting pulmonary condition characterized by reduced air intake, chronic dyspnoea, and a high prevalence rate [1]. In 2020, COPD became the fifth-prevailing morbidity driver, together with being the third-prevailing mortality cause globally [2]. Furthermore, it is frequently associated with comorbidities [3,4]. Therefore, most theoretical views suggest that COPD is a multicomponent disease, often associated with psychological and social issues [5-7].

Many studies have reported that COPD is also related to negative emotions and cognitive impairment, including anxiety and depression, as well as decreased attention, memory, and executive functions, which reduce the patient's quality of life, disease management, and survival [8-10]. In particular, cognitive impairment was associated with higher mortality and disability rates [11,12]. Multiple studies determined cognitive capacity reduction presence within cases of COPD ranges from 10% to 77%, which is significantly higher than that in healthy controls (5% to 24%) [8,13-15]. The wider variations in these estimates are attributed to investigation populations and assessment tools. Cognitive impairment causes in COPD patients is likely to be multifactorial, with a key mechanism proposed being neuronal damage mediated through hypoxia.

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Other factors include smoking, systemic inflammation, vascular disease, and decreased exercise capacity [8,16]. However, the current understanding of cognitive issues in COPD remains inadequate.

Besides medication, pulmonary rehabilitation (PR) is a standard program for regulating and stabilizing COPD, with exercise training being of paramount priority [1]. Several studies reported that regular exercise can improve negative emotions and cognitive capacity within cases of COPD. However, the influence by exercise training on different cognitive and memory functions within COPD remains unclear [10,17-21]. The aim of this investigation was to probe the influence by PR exercise treatment on neurocognitive functions (attention, executive, and memory capacities) and mental health within cases of COPD.

Materials and methods

Study design and participants

This pilot investigation included 28 cases of COPD (FEV_1/FVC <0.7; chronic obstructive lung disease [GOLD] stage ≥ B) from 33 hospitalized cases at Chest Medicine at the Hualien Tzu Chi General Hospital between 2018 and 2019. The institutional review board permitted this investigation (IRB 107-206-A), with all volunteers providing written-informed permission. Based on volunteer rights, all included patients could choose to join either the exercise group or the control group, according to their free will. The exercise group included 12 patients, assigned to receive PR exercise treatment over a 2-month period, while the remaining 16 patients were assigned towards the control group. On 2-month follow-up, the exercise group had completed interventions with good compliance. All patients completed pre and post tests, including the Beck Depression Inventory-II (BDI), Beck Anxiety Inventory (BAI), psychomotor vigilance task (PVT), and Stroop task together with the Wechsler Memory Scale-III Word List Test. The included cases were ≥20 years. The exclusion criteria included patients having a history of –or managed – for any neurological or psychological conditions that could intrude upon neuro-cognitive analytical accuracy, sleep apnea, or neuromuscular conditions, together with cases of not able to finish tasks.

Exercise training program

The exercise group attended a PR exercise training program for 2 months, with two sessions per week, each lasting 50 min. The exercise program was progressive and supervised by a respiratory therapist. The sessions commenced with breathing exercises (pursed lips and diaphragmatic breathing), with subsequent warm-up and 40 min of exercise (ergometer bicycle exercises and strengthening of muscle groups) toward 60%–80% of symptom-limited peak work or pulse rate [1]. Initial resistance was based on cardiopulmonary exercise testing. The control group received identical care and treatment as general outpatients (control group). Both groups were analyzed at baseline and 60-day postenrolment.

Measures

Questionnaires

BDI and BAI scales reflect self-reporting scales. The versions this investigation used were both Chinese versions, having moderate-to-strong validity and reliability [22-24]. BDI consists of 21 questions requiring participants to reply to all questions through a 0–3 score. The patient is required to mark the value reflecting a specific level of feeling experienced within the previous 7 days. The overall score was determined through the addition of scorings for all 21 questions. Scoring 14–19 implied mild depression, 20–28 implied moderate depression, while scoring >29 implied severe depression [25]. BAI is a 21-item tool for determining symptoms of anxiety, having great internal consistency and above-par reproducibility, with scores ranging from 0 to 63. Scoring 8–15 implied mild anxiety, 16–25 implied moderate anxiety, while scoring >26 implies severe anxiety [26].

Investigated analyses

The enrolled participants were asked to complete the computerised PVT and Stroop task. All cognitive assessments were developed through E-prime® 2.0 and construed for generating normative datasets. (Psychology Software Tools, Inc., Sharpsburg, PA, USA).

Psychomotor vigilance task

PVT was developed for assessing sustained attention [27]. Volunteers had to press a button immediately once the counter was visible on-screen for 50 ms. Following this action, reaction time (RT) was visible for 1 s. A random pattern of stimuli with a 2-10 s interstimulus interval occurred. Each test had roughly 114 stimulus presentations lasting 15 min. Before the initial run, individuals completed a single practice test for 1 min. Endpoint indicators investigated were: mean RT (excluding omissions), hit rate, number of lapses (RT >500 ms), omission quantity, and fast rate (RT 500 ms) [28].

Colour-word Stroop task

This was a neuropsychological test that is employed for both experimental and clinical purposes. Previous studies reported that it can measure multiple cognitive functions, such as executive function, processing speed, attention, and cognitive flexibility [29-31]. Participants were given color words (red, blue, yellow, and green) that were printed in complementary color to the word or as an opposite color. Tests that were consistent and those that were not were shown with equal probability. Participants were told to hit one of four answer keys as quickly and accurately as possible as a response to text ink-coloration. Every test began with a fixed cross “+” that was shown for 500 ms before the target was presented, shown for a maximum of 2 s, after which there was a 2-s inter-trial break. Participants conducted two blocks of 72 trials following completing 12 preparation trials, with 1-min rest intervals. The findings of this inquiry were analyzed as follows for trial congruency: mean RT in correct runs, accuracy, error rate, and omission rate [32].

Memory tests

Wechsler memory scale-III word list

The word test included four learning runs of 12 nonsynonymous words, one interference learning run of 12 novel words, a delayed recall run of the first 12 words following 25–35 min with no notice, and a recognition trial [33].

Dataset extraction

Datasets such as age, gender, educational level, spirometry, COPD stage, and medications, were registered. Individuals finished BDI, BAI, PVT, Stroop task, and memory test in identical sequence, in an isolated room, for the test duration of 1.5 h.

Statistical analyses

Datasets reflected means and standard deviations. A comparison of outcomes between baseline and 2 months following PR was performed using the Mann–Whitney *U*-test and Wilcoxon signed rank test as a *post hoc* assessment for pairwise comparisons. Raw scores for word list test were changed into scale scorings using normative datasets from Taiwanese specimens. P <0.05 was deemed as being statistically significant. SPSS® for Windows (version 25.0; SPSS™, Armonk, NY, USA) was employed for all such analyses.

Results

Demographic datasets

As depicted in Table 1, there existed nil variations across anthropometric features for the exercise group and controls. Most participants were 60-year-old men in both groups. Following the Global Initiative for GOLD evaluation, >50% of participants had moderate, followed by severe, mild, and very severe COPD. The two groups were below the mean in several cognition tests. Performance on memory, attention, and executive functions were less successful. Furthermore, mild depression and anxiety impairments were found within cases of COPD [Table 2].

Effects of pulmonary rehabilitation exercise upon mental health

Table 3 presents endpoints for emotion assessment. The exercise group saw a substantial reduction in depression severity as measured by the Beck Inventory test (P < 0.01); however, there was no alteration within the control group. Similar to this, the exercise group saw a substantial improvement within the anxiety trend (P < 0.01). The control group, nevertheless, showed no modifications [Table 3].

Effects of exercise on cognitive function

During the word-list test, immediate memory and recognition significantly increased after 2 months of PR exercise (P < 0.05 and P < 0.001). Although this investigation found a major amelioration within posttest learning rate and delayed memory for the exercise group, no major variations were observed once compared with the control group [Table 4]. Within the Stroop examination, there were no discernible changes across groups in terms of omission rate, mistake rate, accuracy rate, or RT. Compared to patients within the control group, those within the exercise group had significantly improved hit and omission rates within the PVT test. Notably, RT within the control group increased significantly during the posttest period [Table 4].

Discussion

This pilot investigation elucidated that within cases of COPD, immediate memory, learning rate, attention, and executive functions were below average. Furthermore, mild depression and anxiety impairments were observed in these participants. Importantly, participation in a 2-month PR exercise program improved not only memory and attention, but also depression severity and anxiety, when compared to control group patients.

Patients with COPD often experience negative emotions, including depression, and anxiety [34]. PR is a standard program for stabilizing COPD, and regular exercise can improve negative emotions [1]. Previous studies regarding

Table 1: Demographics and baseline characteristics

Variables	Experimental group (*n*=12)	Control group (*n*=16)	*P*
Age (years), mean (SD)	64.67 (14.67)	60.31 (7.94)	0.063
Sex (% men)	91.7	93.8	1
Education, *n* (%)			
No education	1 (8.3)	0	0.738
Elementary school	4 (33.3)	4 (25)	
Junior high school	2 (16.7)	5 (31.3)	
High school	3 (25)	4 (25)	
Junior college or above	2 (16.7)	3 (18.8)	
FEV_1/FVC %, mean (SD)	47.98 (13.03)	54.64 (14.21)	0.312
FEV_1% predictor, mean (SD)	55.1 (18.7)	64.86 (21.57)	0.335
COPD stages, *n* (%)			
Stage 1-Mild	1 (8.3)	4 (25)	0.315
Stage 2-Moderate	7 (58.3)	8 (50)	
Stage 3-Severe	3 (25)	4 (25)	
Stage 4-Very severe	1 (8.3)	0	
Medication, *n* (%)			
LAMA	1 (8.3)	3 (18.8)	0.501
LABA + LAMA	4 (33.3)	9 (56.3)	
LABA + ICS	5 (41.7)	2 (12.5)	
LABA + LAMA + ICS	2 (16.6)	2 (12.5)	

SD: Standard deviation, COPD: Chronic obstructive pulmonary disease, FEV_1: Forced expiratory volume in 1 s, FVC: Forced vital capacity, ICS: Inhaled corticosteroids, LAMA: Long-acting muscarinic antagonists, LABA: Long-acting beta-agonist

Table 2: Baseline characteristics of cognitive capacity and emotional state

Variables	Mean (SD)		P
	Rehabilitation group (n=12)	Control group (n=16)	
Word list			
Immediate memory	9.83 (1.46)	9.38 (2.60)	0.192
Learning rate	9.5 (3.1)	9.44 (2.42)	0.562
Delayed memory	10.17 (3.32)	10.19 (1.75)	0.487
Recognition	10.92 (3.26)	9.94 (2.43)	0.761
Stroop task			
AR (%)	79.29 (16.66)	79.42 (16.43)	0.961
ER (%)	9.72 (9.63)	10.5 (11.89)	0.752
OR (%)	10.98 (10.17)	10.06 (13.12)	0.224
Correct RT (ms)	1070 (216)	1090.35 (207.46)	0.698
PVT			
FR (%)	64.91 (35.27)	60.36 (38.87)	0.696
OR (%)	17.25 (21.26)	13.21 (16.59)	0.534
LR (%)	35.08 (35.27)	39.63 (38.87)	0.696
HR (%)	82.74 (21.26)	86.78 (16.59)	0.534
RT (ms)	459 (260)	509.69 (301.01)	0.854
BAI	11 (6.25)	10.5 (6.62)	0.730
BDI	14.42 (11.15)	13.81 (9.92)	0.596

SD: Standard deviation, AR: Accurate rate, BAI: Beck anxiety inventory, BDI: Beck depression inventory, ER: Error rate, FR: Fast rate, HR: Hit rate, LR: Lapse rate, PVT: Psychomotor vigilance task, OR: Omission rate, RT: Reaction time

Table 3: Changes in emotional state of rehabilitation and control groups after 2 months

Variables	Mean (SD)				P
	Rehabilitation group (n=12)		Control group (n=16)		
	Pretest	Posttest	Pretest	Posttest	
BDI	11 (6.25)	5.83** (5.39)	10.5 (6.62)	13.75 (6.52)	0.005**
BAI	14.42 (11.15)	7.25** (8.97)	13.81 (9.92)	16.06 (9.74)	0.005**

**P<0.01. Wilcoxon signed rank test for within group changes. Data are shown as mean (SD). P: Mann–Whitney test, rehabilitation compared to control. BAI: Beck anxiety inventory, BDI: Beck depression inventory, SD: Standard deviation

the relationship between exercise and emotion demonstrated that exercise can improve depressive symptoms when used as an adjunct to medication [35]. Exercise has been found to lower anxious sensations, even if research on its impact on depression has been more thorough [36,37]. However, little is known about how exercise affects anxiety. Numerous studies have demonstrated that endorphins, mitochondria, the mammalian target of rapamycin, neurotransmitters, the hypothalamic-pituitary-adrenal axis, and the thermogenic hypothesis are among the physiological and biochemical processes through which exercise influences emotional states [19]. In addition, patients' symptoms can be reduced by frequent social interaction and support by using exercise as a diversion from thought patterns, an improvement in self-efficacy, and a reduction in symptoms [38]. After 2 months of PR exercise, Paz-Daz *et al*. observed that the degree of depression in patients of COPD dramatically decreased [39]. A meta-analysis research by Gordon *et al*. was published with the same conclusion. Anxiety and depression symptoms both benefited significantly by PR to a moderate and big extent, respectively. The length of the program had no bearing on the effects [40]. Tselebis *et al*. also reported similar results, stating that anxiety and depression symptoms were significantly reduced in patients post-PR exercise [41]. Cumulatively, the investigation is consistent with the findings of these studies, although a meta-analysis recently found opposing findings. This investigation demonstrated that only a mild relationship existed between physical activity and depression, though not any relationship with anxiety [42]. There may be unidentified factors, such as encouragement from an exercise therapist, that may indirectly affect negative emotional performance in COPD patients.

Attention, perception, memory, learning, language, and executive functions are only a few of the several cognitive processes involved in cognition. Each area has certain operations that offer people both fundamental and sophisticated talents [43]. Numerous individuals with COPD show cognitive impairment in a variety of cognitive domains, including executive functioning, memory, and attention, according to earlier research [14]. Using a neuropsychology exam, Cleutjens *et al*. evaluated the performance of 90 COPD patients with a control group. They discovered that individuals with COPD frequently showed cognitive flexibility, planning, and psychomotor speed issues [44]. Liesker discovered that COPD patients had difficulties with activities that largely assessed the speed of information processing [16]. Furthermore, according to several studies [45-47], memory loss in COPD patients was not caused by alterations in the aging process. Numerous research [8,14] suggest a link between deteriorating clinical state and cognitive impairment. Cognitive impairment may impact self-management and treatment adherence [48]. In addition to increasing the risk of dropping out of the PR program, it may also interfere with the course of respiratory therapy [49].

Although some studies probed possible associations across PR exercise programs and improved cognitive assessment, little is known regarding the benefits to specific cognitive domains within cases of COPD. Etnier and Berry found that cognitive capacity and walking distance improved significantly within cases of COPD following 3 months of exercise [17]. Several studies reported that PR exercise programs had a beneficial influence on cognitive capacity, especially within COPD cases having cognitive impairment [10,21]. Pereira *et al*. demonstrated that participation in a 3-month comprehensive multidisciplinary PR program was associated with improvement in verbal learning and cognitive processing speed post adjusting for age, sex, tobacco consumption, and educational level [50]. The current investigation found that patients with COPD could benefit from a 2-month exercise training session, including immediate verbal and recognition memory and emotional status. Several physiological mechanisms may have contributed to these improvements. Exercises for rehabilitation have been suggested to improve cognitive functions in COPD patients through a number of mechanisms, including an increase in blood flow to the brain, an increase in the transport and use of oxygen within the

Table 4: Changes in cognitive capacity of rehabilitation and control groups after 2 months

Variables	Mean (SD)				*P*
	Rehabilitation group (*n*=12)		Control group (*n*=16)		
	Pretest	Posttest	Pretest	Posttest	
Word list					
Immediate memory	9.83 (1.46)	13.25** (3.16)	9.38 (2.60)	10.5 (2.28)	0.026*
Learning rate	9.5 (3.1)	11.5** (3.58)	9.44 (2.42)	9.56 (2.44)	0.147
Delayed memory	10.17 (3.32)	11.92* (3.47)	10.19 (1.75)	10.25 (1.84)	0.083
Recognition	10.92 (3.26)	13.08* (1.24)	9.94 (2.43)	9.44 (2.44)	0.000***
Stroop task					
AR (%)	79.29 (16.66)	89.39* (9.1)	79.42 (16.43)	83.41 (15.03)	0.374
ER (%)	9.72 (9.63)	7.89 (7.42)	10.5 (11.89)	11.63 (14.85)	0.748
OR (%)	10.98 (10.17)	2.71* (3.51)	10.06 (13.12)	4.94 (5.69)	0.172
Correct RT (ms)	1070 (216)	1009 (169)	1090 (207)	1085 (225)	0.348
PVT					
FR (%)	64.91 (35.27)	79.60 (27.22)	60.36 (38.87)	45.72 (39.92)	0.037*
OR (%)	17.25 (21.26)	8.11* (9.10)	13.21 (16.59)	19.53 (17.32)	0.033*
LR (%)	35.08 (35.27)	20.39 (27.22)	39.63 (38.87)	54.27 (39.92)	0.037*
HR (%)	82.74 (21.26)	91.88* (9.10)	86.78 (16.59)	81.46 (17.2)	0.033*
RT (ms)	459 (260)	365 (172)	509 (301)	656* (361)	0.023*

*$P<0.05$, **$P<0.01$, ***$P<0.001$. Wilcoxon signed rank test for within group changes. Data are shown as mean (SD). *P*: Mann–Whitney test, rehabilitation compared to control. AR: Accurate rate, ER: Error rate, FR: Fast rate, HR: Hit rate, LR: Lapse rate, PVT: Psychomotor vigilance task, OR: Omission rate, RT: Reaction time, SD: Standard deviation

brain's environment, the release of neurotransmitters, and an increase in brain-derived neurotrophic factors to support brain plasticity [8,10].

This investigation found a significant increase in immediate verbal/recognition memory following 2 months of PR exercise. Within the PVT test (lower-order cognitive function), the omission rate decreased while the hit rate increased significantly, indicating an improvement in attention performance. However, the difference within Stroop test scorings (higher-order cognition and executive function) was not significant. Executive capacity is the capability to organize, start, sequence, monitor, and inhibit complicated tasks aimed at goals. It is assumed that particular frontal circuits govern executive capacity [51]. Substantial metabolic deterioration has reportedly been noted in the cerebral cortex of patients with COPD, according to several investigations [51,52]. Given the potential impacts of long-term chronic hypoxia in COPD patients, frontal circuit elements are especially vulnerable to hypoperfusion and hypoxia [53]. In addition, studies have reported that post-PR, the cognitive ability of patients may not be improved comprehensively [10,21,54]. Overall, these results extend those of previous studies and showed that patients with COPD had below average cognitive capacity and that PR could improve lower-order cognitive capacity performance.

Study limitations

There are various restrictions on this inquiry. First, there was just one center used for the inquiry, which was minimal. Despite identical baseline data for matched groups, this experiment was a nonrandomized test, and outcomes might have been influenced by motivation, expectations, etc., These findings need to be confirmed by more large-scale research and multicenter trials. Second, a fit group was not included in this study. This study used the Taiwan memory data for the normative memory test in order to overcome this restriction. The calculated cognitive tasks of the PVT and Stroop test, however, lacked normative datasets. Consequently, results from the cognitive tasks should be evaluated carefully. Third, it was unable to ascertain the degree to which changes in exercise capacity and dyspnea were linked to changes in cognitive function before and after rehabilitation. These elements could have been modified following rehabilitation. Fourth, this study omitted information on these individuals' SpO_2 levels at rest and their oxygen desaturation levels after activity. Hypoxemia is correlated with cognitive impairment within cases of COPD and can influence on the improvements derived from exercise intervention.

Conclusions

The current study demonstrated that a 2-month PR exercise program significantly improved negative emotions and many cognitive domains. However, it remains unclear how long this impact will last. In any case, these findings imply that PR exercise could be advantageous for cognitive function and depressive mood.

Data availability statement

The complete dataset is included in this manuscript.

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Conflicts of interest

Dr. En-Ting Chang, an editorial board member at *Tzu Chi Medical Journal*, had no role in the peer review process of or decision to publish this article. The other authors declared no conflicts of interest in writing this paper.

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