

Improvements in functional and cognitive status following a short-term pulmonary rehabilitation in COPD lung-transplant recipients – A pilot study

Online Data Supplement

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Neuropsychological Testing battery

A comprehensive neuropsychological assessment battery was used for the LTx-recipients cognitive assessment including the following clinical tools in *German version* on PR admission and at discharge: 1) *Wechsler Memory Scales IV*: Logical Memory I [LG1], Logical Memory II [LG2] [1], 2) *California Verbal Learning Test (CVLT)*: word learning [LS], reading section 1 [DG1], reading section 5 [DG5], word list for interference effect [LB], delayed free repetition [VFW], repetition with help [WA], and repetition errors [W] [2]; 3) *Test battery of attentional performance (TAP)*: Index of Speed- Accuracy- Trade off [ISAT %], Divided attention performance [GAA %] [3]; 4) *Trail Making Test (TMT)*: Test version A [TMT-A sec], Test version B [TMT-B sec] [4]; 5) *Stroop test - colour word interference*: colour-word read [FWL], colour recognition [FSB], interference performance [INT] [5]; 6) *Behavioural Assessment of the Dysexecutive Syndrome (BADS test)*: Test version A [BV-1], Test version B [BV-2] [6]; 7) Clock-drawing test [7] (Please see Figure 1 and online supplement for more details). Multiple scores achieved in the administered cognitive tests determined the evaluation of cognitive performance for the following domains: *a) Memory ability, b) Learning skills, c) Attention and flexibility, d) Psychomotor speed, e) Behavioural activation, f) Visuospatial and processing speed, and g) Visuospatial and praxis*. One composite score for each of the cognitive domains was calculated by adding all the mean achieved scores from the cognitive tests that correspond to certain cognitive domains (Online table 3).

Six-minute walk test

The 6MWT was performed according to international recommendations [8, 9]. Briefly, participants were asked to walk indoors on a flat, straight, 30-meter walking course as far as they can under the supervision of a well-trained researcher. Blood oxygen saturation (SpO₂), dyspnea and leg-fatigue (Borg-scale) were assessed. Distance-saturation product (DSP) was calculated as the product of the final distance walked in meters and the post-exercise SpO₂% (DSP m% = 6MWD m × SpO₂%post /100) [10]. Unintended stop points were defined as a (temporary) discontinuation of the 6MWT [11].

Supplementary tables

Online table 1. Cognitive tests categorized based on the evaluation of different cognitive domains			
Memory ability	Learning skills	Attention & flexibility	Psychomotor speed
Wechsler Memory Scales IV: [LG1]	California Verbal Learning Test: [LS1]	Test battery of Attentional Performance: [ISAT1]	Stroop test – colour-word interference: [FWL]
Wechsler Memory Scales IV: [LG2]	California Verbal Learning Test: [DG1]	Test battery of Attentional Performance: [GAAP1]	Stroop test – colour-word interference: [FSB]
California Verbal Learning Test: [VFW1]	California Verbal Learning Test: [DG5]		Stroop test – colour-word interference: [INT]
California Verbal Learning Test: [VFW2]	California Verbal Learning Test: [LB]		
California Verbal Learning Test: [WA1]			
California Verbal Learning Test: [WA2]			
California Verbal Learning Test: [W]			
Behavioural activation	Visuospatial & processing speed	Visuospatial & praxis ability	
Behavioural Assessment of the Dysexecutive Syndrome: [BADS- BV1]	Trail Making Test: [TMT-A]	Clock-Drawing Test: [Uhr-Test]	
Behavioural Assessment of the Dysexecutive Syndrome: [BADS- BV2]	Trail Making Test: [TMT-B]		

Online table 1: Domain-specific cognitive evaluation was performed using these test for each cognitive domain. The sum of the scores in these cognitive tests determined the *composite score* for each corresponding cognitive domain. Within brackets are the abbreviations for the *German version* of the performed cognitive tests.

Online table 2. A single-day exercise training in Pulmonary Rehabilitation program		
Endurance training	Duration	Intensity
Bicycle ergometer	20 minutes	70% of peak work rate
Strength training	Repetitions	Intensity
Leg press		
Knee extension		
Hip abduction/adduction	3 set X	Individual load is set to reach momentary muscular failure at the end of each set
Shoulder Pull Down	15 repetitions	
Rowing		
Abdominal muscles		
<i>Estimated duration: 30 minutes</i>		
Activities of daily living training	Duration	Intensity
walking training and/or calisthenics exercises using body weight, small dumb-bells, rubber tubes etc.	30 minutes	Low to moderate individual exertion

Online table 2: Elements of the exercise training of the implemented 3-week PR program in LTx-recipients for COPD.

Online table 3. Pearson's correlations amongst cognitive tests performance and health and mental status						
	HADS Anxiety	HADS Depression	CRQ Dyspnea	CRQ Fatigue	CRQ Emotion	CRQ Mastery
Memory ability						
WMS Logical Memory I	0.11	-0.09	0.19	0.01	0.01	0.05
WMS Logical Memory II	0.07	0.12	0.17	-0.06	0.04	-0.02
CVLT Free recall – list 1	0.42	-0.37	0.10	0.08	0.19	0.21
CVLT Free recall – list 2	-0.44	-0.16	0.22	0.25	0.30	0.30
CVLT Recall with help- List 1	-0.36	-0.08	0.48	0.26	0.47	0.43
CVLT Recall with help- List 2	-0.62**	-0.43	0.47	0.26	0.42	0.40
CVLT Repeating errors	-0.06	-0.48	-0.22	-0.08	-0.16	-0.02
Learning skills						
CVLT Learning ability, %	-0.46	-0.19	0.22	0.15	0.25	0.22
CVLT Passage 1, %	-0.24	0.05	-0.04	0.14	0.24	0.24
CVLT Passage 5, %	-0.52*	-0.43	0.47	0.34	0.34	0.38
CVLT List B, %	0.02	0.33	0.03	0.07	0.18	0.11
Attention & Flexibility						
TAP Speed / accuracy, %	0.26	-0.16	-0.44	-0.37	-0.15	-0.28
TAP Shared attention, %	0.13	0.17	-0.04	0.01	-0.02	0.11
Visuospatial & processing						
TMT - A, score	0.46	0.15	-0.27	-0.25	-0.20	-0.17
TMT - B, score	0.06	-0.02	-0.33	-0.31	-0.29	-0.15
Visuospatial & praxis ability						
CDT Clock test	0.30	0.29	-0.18	-0.03	-0.03	-0.12
Psychomotor Speed						
Stroop colour-word read	-0.22	0.27	0.29	0.23	0.24	0.15
Stroop colour recognition	-0.45	-0.23	0.50*	0.28	0.24	0.27
Stroop interference	-0.03	0.11	0.11	-0.03	-0.11	-0.06
Behavioural activation						
BADS version 1	0.21	0.17	0.09	-0.22	-0.32	-0.28
BADS version 2	0.32	0.21	0.21	0.26	0.19	0.22

Online table 3: Pearson's correlations (r) amongst cognitive, mental, and health status tests. Asterisks denote significance (* $p < 0.05$, ** $p < 0.001$).

Online table 4. Demographics and clinical characteristics after stratification by single- and bilateral- LTx

Clinical characteristics	All Patients (n=24)	Single-LTx (n=8, 33%)	Double-LTx (n=16, 67%)	P Value
Women, n, (%)	10 (42)	3 (37)	7 (44)	NS
Age, years, \pm SD	58.2 \pm 6.3	62.4 \pm 4.7	56.1 \pm 6.1	0.019
Height, m	1.71 \pm 0.09	1.74 \pm 0.08	1.70 \pm 0.09	NS
Weight, kg	64.6 \pm 12.1	64.7 \pm 12.7	64.5 \pm 12.4	NS
BMI kg·m ²	22.0 \pm 3.5	21.5 \pm 4.0	22.2 \pm 3.4	NS
FEV ₁ , %pred.	75.4 \pm 22.0	54.3 \pm 10.4	86.6 \pm 17.8	<0.001
DLCO, %	53.5 \pm 16.4	38.3 \pm 8.5	58.6 \pm 16.4	0.019
RV/TLC, %	55.6 \pm 12.1	66.3 \pm 3.7	49.9 \pm 11.1	<0.001
CRQ dyspnea, score	4.7 \pm 2.1	4.3 \pm 1.9	5.0 \pm 2.3	NS
CRQ fatigue, score	4.9 \pm 1.5	4.9 \pm 1.6	4.9 \pm 1.5	NS
CRQ emotion, score	5.5 \pm 1.4	5.4 \pm 1.3	5.6 \pm 1.6	NS
CRQ mastery, score	5.8 \pm 1.4	5.6 \pm 1.6	6.0 \pm 1.4	NS
HADS anxiety, score	4.4 \pm 4.2	4.4 \pm 3.6	4.4 \pm 4.7	NS
HADS depression, score	3.8 \pm 3.5	4.9 \pm 4.6	3.1 \pm 2.5	NS
Education, years	8.0 \pm 2.6	7.9 \pm 2.7	8.1 \pm 2.6	NS
IQ, score	110.0 \pm 12.4	109.1 \pm 11.3	110.4 \pm 13.2	NS
6MWD, m	346 \pm 127	321 \pm 152	349 \pm 122	NS
6MWD, %pred.	51.0 \pm 17.7	51.8 \pm 17.4	50.6 \pm 18.5	NS
DSP, m%	326 \pm 124	299 \pm 146	333 \pm 115	NS
Unintended stop point, m	340 \pm 130	321 \pm 153	349 \pm 122	NS

Online table 4: Differences in clinical characteristics after stratification by single- and bilateral- LTx. Data are mean \pm SD unless specified otherwise. Level of significance was set at $P \leq 0.05$.

References

1. Lepach AC, Petermann F. [Cognitive function assesment by Wechsler Memory Scale – Fourth Edition]. *Z Neuropsychol* 2012; **23**: 123-132.
2. Niemann H, Sturm W, Thoene-Otto A, Willmes K. CVLT California Verbal Learning Test, German Adaptation. Manual. Hogrefe, Frankfurt, Germany, 2008.
3. Zimmermann P, Fimm B. [Divided attention: Test of Attentional Performance (TAP, Version 2.2)]. *Vera Fimm Psychologische Testsysteme*, Herzogenrath, Germany, 2002.
4. Rodewald K, Bartolovic M, Debelak R, Aschenbrenner S, Weisbrod M, Roesch-Ely D. [A standardization study of a modified trail making test in German-speaking countries]. *Z Neuropsychol* 2012; **23**: 37-48.
5. Bäumler G. [Colour-Word Interference of J.R. Stroop: instructions] *Psychologie Hogrefe* 1985.
6. Wilson BA, Alderman N, Burgess PW, Emslie HC, Evans JJ. The behavioural assessment of the dysexecutive syndrome. Thames Valley Test Company, Flempton, Bury St. Edmunds, 1996.
7. Shulman KI. Clock-drawing: is it the ideal cognitive screening test? *Int J Geriatr Psychiatry* 2000; **15**: 548-561.
8. Holland AE, Spruit MA, Troosters T, et al. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. *Eur Respir J.* 2014; **44**: 1428-1446.
9. Singh SJ, Puhan MA, Andrianopoulos V, et al. An official systematic review of the European Respiratory Society/American Thoracic Society: measurement properties of field walking tests in chronic respiratory disease. *Eur Respir J.* 2014; **44**: 1447-1478.32.78.
10. Lettieri CJ, Nathan SD, Browning RF, Barnett SD, Ahmad S, Shorr AF. The distance-saturation product predicts mortality in idiopathic pulmonary fibrosis. *Respir Med* 2006; **100**: 1734-1741.
11. Andrianopoulos V, Wouters EF, Pinto-Plata VM, et al. Prognostic value of variables derived from the six-minute walk test in patients with COPD: Results from the ECLIPSE study. *Respir Med.* 2015; **109**: 1138-1146.